

**EPA Registration Number**  
**11556-117 vol. 3**

# Material Sent for Data Extraction

Reg. # 11556 - 117

Description: \_\_\_\_\_

☐ Material(s) Sent to Data Extraction Contractors:

☒ New Stamped Label Dated 8/29/12

☐ Notification Dated \_\_\_\_\_

☐ New CSF(s) Dated \_\_\_\_\_

☐ Other: \_\_\_\_\_

☐ Decision #: \_\_\_\_\_

☐ Other Action/Comments: \_\_\_\_\_

File this coversheet and attached materials in the jacket. It must be well organized and clipped together, NOT STAPLED. Then give the jacket with the coversheet and materials to staff in the Information Services Center (ISC) (Room S-4900). If a jacket is full or only available as an image, please file materials in a new jacket and bring it down to the (ISC). For further information please call 703-605-0716.

Reviewer: Autumn Metzger

Phone: 305-5314 Division: RD - IRB

Date: 8/29/12

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460



AUG 29 2012

OFFICE OF CHEMICAL SAFETY  
AND POLLUTION PREVENTION

Douglas Spilker, Ph.D  
Bayer HealthCare LLC, Animal Health Division  
P.O. Box 390  
Shawnee Mission, KS 66201-0390

Dear Dr. Spilker:

Subject: Amendment to update labels per spot on mitigation letter sent by the Agency dated September 30, 2011  
EPA Registration Nos./Product name:  
11556-116, Advantage 9 Topical Solution (small cats)  
→ 11556-117, Advantage 10 Topical Solution (small dogs)  
11556-118, Advantage 18 Topical Solution (large cats)  
11556-119, Advantage 20 Topical Solution (medium dogs)  
11556-120, Advantage 55 Topical Solution (large dogs)  
11556-122, Advantage 100 Topical Solution (extra large dogs)

The labeling referred to above submitted in connection with the Federal Insecticide, Fungicide and Rodenticide, as amended are acceptable.

A stamped copy of the labeling is enclosed for your records. Please submit one final printed copy of the labeling before releasing the product for shipment. If you have any questions regarding this label, please contact Autumn Metzger at (703) 305-5314.

Sincerely,

A handwritten signature in black ink, appearing to read "Venus Eagle", with a long horizontal line extending to the right.

Venus Eagle  
Product Manager 01  
Insecticide-Rodenticide Branch  
Registration Division (7505P)

Reason To Issue: Revise according to EPA "Implementation Date: 08/20/2012  
of Label Changes to Pet Spot-On Products" Supersedes: 07/17/2012,  
document, dated 9/30/11 (Rec'd 10/11/11) 03/01/2012 & 08/27/2010

[Front Panel]

**Advantage® 10 Topical Solution**

Alternate Brand Name: **Advantage for Small Dogs**

Once-A-Month Topical Flea and Lice Treatment  
For Use Only on Dogs and Puppies 7 Weeks and Older and Weighing 3½ to 10 lbs.

**READ THE ENTIRE LABEL BEFORE EACH USE**

For the Prevention and Treatment of Flea and Lice Infestations on Dogs

- One treatment prevents further flea infestation for at least four (4) weeks
- Kills fleas on dogs within 12 hours
- Kills fleas before they lay eggs
- Convenient, easy to apply
- Kills [(biting) (chewing)] lice
- For treatment and prevention of [(biting) (chewing)] lice [infestations]
- Controls existing [(biting) (chewing)] lice infestations
- Dual protection (against fleas and lice)
- Treats, prevents and controls [(biting) (chewing)] lice [infestations]
- Provides effective control of [(biting) (chewing)] lice [infestations]
- Kills [(biting) (chewing)] lice and prevents further infestations
- For treatment and prevention of infestations with [(biting) (chewing)] lice
- Waterproof
- Fragrance free

	<u>% By Weight</u>
Active Ingredient	
Imidacloprid .....	9.1%
Other Ingredients .....	90.9%
Total .....	100.0%
EPA Est. No. 11556-XXX-X	EPA Reg. No. 11556-117

- See Back Panel for First Aid and Precautionary Statements.
- For Directions For Use, and Storage and Disposal (instructions), see supplemental labeling inside.

Icon size 1.5cm x 1.5cm



**KEEP OUT OF REACH OF CHILDREN  
WARNING**

**ACCEPTED  
AUG 29 2012**

**Under the Federal Insecticide, Fungicide,  
and Rodenticide Act, as amended, for the  
pesticide registered under:**



Reason To Issue: Revise according to EPA "Implementation of Label Changes to Pet Spot-On Products" document, dated 9/30/11 (Rec'd 10/11/11) Date: 08/20/2012 Supersedes: 07/17/2012, 03/01/2012 & 08/27/2010

[Back Panel]

## PRECAUTIONARY STATEMENTS

### HAZARDS TO HUMANS

**WARNING:** Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Harmful if swallowed. Do not get in eyes or on clothing. Avoid contact with skin. Wash hands thoroughly with soap and warm water after handling. Keep out of reach of children. Do not contaminate feed or food.

FIRST AID	
If In Eyes:	<ul style="list-style-type: none"><li>• Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye.</li><li>• Call a poison control center or doctor for treatment advice.</li></ul>
If Swallowed:	<ul style="list-style-type: none"><li>• Call a poison control center or doctor immediately for treatment advice.</li><li>• Have person sip a glass of water if able to swallow.</li><li>• Do not induce vomiting unless told to do so by the poison control center or doctor.</li><li>• Do not give anything by mouth to an unconscious person.</li></ul>
If on Skin or Clothing	<ul style="list-style-type: none"><li>• Take off contaminated clothing. Rinse skin immediately with plenty of water for 15 – 20 minutes. Call a poison control center or doctor for treatment advice.</li></ul>
HOT LINE NUMBER	
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. For medical emergencies call 1-800-422-9874. For customer questions call 1-800-255-6826.	
NOTE TO PHYSICIAN	
Treat the patient symptomatically.	

### HAZARDS TO DOMESTIC ANIMALS

**For external use only.** Do not use on puppies under seven weeks of age or weighing less than 3½ lbs. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing dogs. Individual sensitivities, while rare, may occur after using ANY pesticide product for pets. If signs persist, or become more severe, consult a veterinarian immediately. If your animal is on medication, consult your veterinarian before using this or any other product. For consumer questions call 1-800-255-6826. For medical emergencies call 1-800-422-9874.

Reason To Issue: Revise according to EPA "Implementation of Label Changes to Pet Spot-On Products" document, dated 9/30/11 (Rec'd 10/11/11) Date: 08/20/2012  
Supersedes: 07/17/2012, 03/01/2012 & 08/27/2010

**Side Effects:** Monitor your dog after application. Side effects, although very rare, may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as vomiting or diarrhea have also been reported. If these or other side effects (such as lethargy) occur, consult your veterinarian or call 1-800-422-9874.

**DO NOT USE ON CATS.** Keep cats away from treated dogs for 24 hours. If applied to a cat or ingested by a cat, contact your veterinarian.

Icon size 1.5cm x 1.5 cm



**RESTRICTIONS:**

- Use only on dogs 7 weeks and older. Do not use on other animals. Do not apply to puppies or dogs weighing less than 3½ lbs.
- Do not apply more than one (1) tube per treatment.
- Do not have contact or allow children to have contact with treated area until completely dry.

Net Contents: [X] Tube(s) each 0.014 fl. oz. (0.4 mL)  
[Sample – Not for (Re)Sale]

Manufactured For  
Bayer HealthCare LLC  
Animal Health Division  
P.O. Box 390  
Shawnee Mission, Kansas 66201 USA

Made in Germany

Reason To Issue: Revise according to EPA "Implementation of Label Changes to Pet Spot-On Products" document, dated 9/30/11 (Rec'd 10/11/11) Date: 08/20/2012 Supersedes: 07/17/2012, 03/01/2012 & 08/27/2010

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[Back Panel and/or insert]

### ***DIRECTIONS FOR USE***

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling.

#### **HOW TO APPLY**

1. Remove one applicator tube from the package.
2. Hold applicator tube in an upright position facing away from you and your pet's face and eyes. Pull cap off tube.

[Visuals Depicting How to Open Applicator Tube]

3. Turn the cap around and place other end of cap back on tube.
4. Twist cap to break seal, then remove cap from tube.
5. The dog should be standing for easy application. Part the hair on the dog's back, between the shoulder blades, until the skin is visible. Place the tip of the tube on the skin and squeeze the tube to expel the entire contents directly on the skin. *Do not get this product in your dog's eyes or allow your dog to ingest this product.* Do not allow the product to run off.

[Visuals Depicting Application To Animal]

6. Discard empty tube as described in Storage and Disposal.
7. In case of severe flea infestation, retreatment may be necessary earlier than four weeks. Do not retreat more often than once every seven days. After flea control is attained, return to a monthly retreatment schedule.

#### **PRODUCT INFORMATION**

The successive feeding activity of fleas on dogs may elicit a hypersensitivity skin disorder known as flea allergy dermatitis (FAD). Treatment of dogs with Advantage kills fleas and may reduce the incidence of this condition.

Reason To Issue: Revise according to EPA "Implementation of Label Changes to Pet Spot-On Products" document, dated 9/30/11 (Rec'd 10/11/11) Date: 08/20/2012 Supersedes: 07/17/2012, 03/01/2012 & 08/27/2010

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Advantage kills fleas on dogs within 12 hours. Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting for up to four (4) weeks. Pre-existing pupae in the environment may continue to emerge for six (6) weeks or longer depending upon the climatic conditions.

Larval flea stages in the dog's surroundings are killed following contact with an Advantage treated dog.

Advantage is waterproof and remains effective following a shampoo treatment, swimming or after exposure to rain or sunlight.

Monthly treatments are required for optimal control and prevention of fleas.

#### **STORAGE AND DISPOSAL**

Do not contaminate water, food or feed by storage or disposal.

**Pesticide Storage:** Store in a cool, dry place inaccessible to children and pets. **Pesticide Disposal and Container Handling:** Nonrefillable container. **If empty:** Do not reuse or refill this container. Place in trash or offer for recycling if available. **If partly filled:** Call your local solid waste agency or 1-800-422-9874 for disposal instructions. Never place unused product down any indoor or outdoor drain.

#### **LIMITED WARRANTY AND LIMITATION OF DAMAGES**

Bayer HealthCare LLC, Animal Health Division warrants that this material conforms to the chemical description on the label. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, BAYER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY, INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR MERCHANTABILITY, and no agent of Bayer is authorized to do so except in writing with a specific reference to this warranty. Any damages arising from a breach of this warranty shall be limited to direct damages and shall not include consequential commercial damages such as loss of profits or values, etc.

Reason To Issue: Revise according to EPA "Implementation of Label Changes to Pet Spot-On Products" document, dated 9/30/11 (Rec'd 10/11/11) Date: 08/20/2012 Supersedes: 07/17/2012, 03/01/2012 & 08/27/2010

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[Label on Individual Tube]

Advantage® 10

9.1% Imidacloprid

0.014 fl. oz. (0.4 mL)

EPA Reg. No. 11556-117

WARNING

Keep Out of Reach of Children

Read The Entire Label Before Use

BAYER

Lot No. 0000000

Reason To Issue: Revise according to EPA "Implementation of Label Changes to Pet Spot-On Products" document, dated 9/30/11 (Rec'd 10/11/11) Date: 08/20/2012  
Supersedes: 07/17/2012, 03/01/2012 & 08/27/2010

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[Label on blister card; one card containing 1, 2, 3, 4, 5 or 6 tubes]

Advantage® 10  
Topical Solution

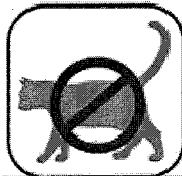
For external use only on dogs and puppies 7 weeks and older and weighing 3½ to 10 lbs.

9.1% Imidacloprid

[X] - 0.014 fl. oz. (0.4 mL)

EPA Reg. No. 11556-117

BAYER



11556-117



**FW: Advantage labels - revised (EPA Reg. Nos. 11556-116, -117, -118, -119, -120, -122)**

**Doug Spilker** to: Autumn Metzger

Cc: Venus Eagle

08/27/2012 11:07 AM

History: This message has been replied to.

*originally  
all  
received  
8/20*

Hi Autumn,

I haven't heard from you regarding this submission. I assumed you received these. I am working on the next batch this week. Any further comments that would affect Advantage II would be appreciated.

Best Regards,  
Doug

Douglas A. Spilker, Ph.D.  
Manager - EPA Reg. Affairs  
BAYER HEALTHCARE LLC  
Animal Health Division  
Office: 913-268-2751  
Mobile: 816-506-3102  
Email: doug.spilker@bayer.com

Address:  
P.O. Box 390  
Shawnee Mission, KS 66201-0390  
Country: USA

Bayer Animal Health "Protecting.Curing.Caring...Together"

From: Doug Spilker  
Sent: Thursday, July 19, 2012 11:31 AM  
To: Autumn Metzger  
Subject: Advantage labels - revised (EPA Reg. Nos. 11556-116, -117, -118, -119, -120, -122)

Hi Autumn,  
Here is this batch. I think I captured everything.

I am still working on the others.

Best Regards,  
Doug

Douglas A. Spilker, Ph.D.  
Manager - EPA Reg. Affairs  
BAYER HEALTHCARE LLC  
Animal Health Division  
Office: 913-268-2751  
Mobile: 816-506-3102  
Email: doug.spilker@bayer.com

Re: Advantage labels - revised (EPA Reg. Nos. 11556-116, -117, -118, -119, -120, -122) □

Autumn Metzger to: Doug Spilker

07/25/2012 08:06 AM

Hi Doug,

Almost there.

**On all of the labels:**

- We still need to add something that says "Front Panel" since that is our only way to be certain what you put under it will actually get on the front panel. So, at the top of the entire label add this.
- Under Restrictions, revise each first bullet so that they indicate ONLY on dogs/cats over XXX weeks old and over XXX lbs (well depend on the wording whether its over or under so make sure they each make sense since they're all a little different)
- On the blister cards, you must add the word "ONLY" to the sentence indicating the weight/age again. So they should read "For external use only on dogs/cats...."

**other specific comments -**

11556-122 - under restrictions, for the second bullet you need to add specific language similar to what we added on the large cat size to indicate that *regardless of size* you only apply 1 tube per treatment

11556-118 - pg 3, under restrictions, revise the first bullet to read 9 lbs (not 2 lbs) and be sure to add the part about "or under 8 weeks old" as stated above

11556-119, -117, - 116 and -118

under the directions for use, add the statement "do not allow product to runoff"

Autumn Metzger  
Biologist  
U.S. Environmental Protection Agency  
Insecticide-Rodenticide Branch  
Registration Division (7505P)  
1200 Pennsylvania Ave. NW  
Washington, DC 20460

Tel: 703 305-5314

Fax: 703 308-5433

Email: metzger.autumn@epa.gov

Doug Spilker

Hi Autumn, Here is this batch. I think I captured...

07/19/2012 12:31:48 PM

From: Doug Spilker <doug.spilker@bayer.com>  
To: Autumn Metzger/DC/USEPA/US@EPA  
Date: 07/19/2012 12:31 PM  
Subject: Advantage labels - revised (EPA Reg. Nos. 11556-116, -117, -118, -119, -120, -122)

---

Hi Autumn,  
Here is this batch. I think I captured everything.

I am still working on the others.



11556-116-122 and 11556-125-151 spot on mitigation amendments

Autumn Metzger

to:

Doug Spilker

07/16/2012 02:39 PM

Hide Details

From: Autumn Metzger/DC/USEPA/US

To: "Doug Spilker" <doug.spilker@bayer.com>

Hi Doug,

Per the original batch 11556-116-122 regarding your rebuttal and resubmission of 11556-122 to be used as a model for the rest:

pg 2 (Back panel) - needs the "WARNING" and "KROC" again with the "Precautionary Statements"

pg 2 -Hazards to Humans -

In reponse to your comment about this being a "uni-dose" and used in "very small volumes (largest being 2.5 ml). The acute tox eye test used only .1ml, a fraction of even the smallest uni-dose size. Therefore, you may leave off the goggle part to keep a level playing field with the products you cited, however for the protection of your users it is still advised to keep it.

In response to your comment about the LRM being guidance. It is a guidance document that cites mandatory language requirements, as is the language for the hazards to humans. Therefore revise as stated before: "Causes substantial buy temporary eye injury. Do not get in eyes or on clothing. Harmful if swallowed...."

pg 2 - the cat warning is required to be 1.5 cm x 1.5 cm. I see it is correct on the final printed, however as the stamped label is the law, all requirements must be on what will end up being the stamped label.

pg 3, move the First Aid box under the Hazards to Humans section.

pg 5, the company name and address must appear on the front or back panel

pg 7, you have the blister card saying "[6][4][1]" but are these on individual blisters? or is this written across all 4 or 6 at once?

pg 7, add the epa reg number to the blister cards

11556-125-151 -

apply all changes discussed for last round and in the above comments (with the exception of the acute tox since those studies were different and the language on the labels is okay).

In addition:

11556-152, page 5, revise the statement "For cats over 9 lbs, do not apply more than 1 tube per treatment" to read (and be bold) "For cats much heavier than 9 lbs, still only apply 1 tube per treatment" (or something to the effect to explain better that very large cats still get 1 tube...)

11556-150, is the name "Advantage II Kitten" misleading since cats up to 5 lbs can use it too? (I see you say later "cats" but just wondering)

11556-151, page 2, revise second sentence under hazards to domestic animals to read "Do not apply to cats or kittens under 8 weeks of age OR under 5 lbs.

Feel free to call me tomorrow any time if you want to discuss or clarify anything I listed.

thanks,

Autumn Metzger  
Biologist  
U.S. Environmental Protection Agency  
Insecticide-Rodenticide Branch  
Registration Division (7505P)  
1200 Pennsylvania Ave. NW  
Washington, DC 20460

Tel: 703 305-5314  
Fax: 703 308-5433  
Email: metzger.autumn@epa.gov



**RE: Amendment for spot on mitigation for EPA Reg Nos. 11556-116, 11556-117, 11556-118, 11556-119 & 11556-122**

**Doug Spilker** to: Autumn Metzger

07/03/2012 02:35 PM

Cc: Venus Eagle

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History: This message has been replied to.

Hi Autumn,

Please find attached a draft label for Advantage 100 (Example) showing the revisions we plan to make, based on our discussions. Furthermore, please also find attached a discussion document that outlines the changes and/or provides information regarding our position on other changes requested of Bayer for these products. My plan is to revise the rest of the draft labels as soon as we reach an understanding on the attached example label. I should be able to reply with the rest of the labels within a week once agreement is reached. I am out tomorrow (of course) plus Thursday and Friday. If we cannot discuss this afternoon, then Monday morning would be the earliest.

Have a good 4th, if we do not talk.

Best Regards,  
Doug

Douglas A. Spilker, Ph.D.  
Manager - EPA Reg. Affairs  
BAYER HEALTHCARE LLC  
Animal Health Division  
Office: 913-268-2751  
Mobile: 816-506-3102  
Email: doug.spilker@bayer.com

Address:  
P.O. Box 390  
Shawnee Mission, KS 66201-0390  
Country: USA

Bayer Animal Health "Protecting.Curing.Caring...Together"

From: Autumn Metzger [mailto:Metzger.Autumn@epamail.epa.gov]  
Sent: Wednesday, June 06, 2012 12:49 PM  
To: Doug Spilker  
Cc: Venus Eagle  
Subject: Amendment for spot on mitigation for EPA Reg Nos. 11556-116, 11556-117, 11556-118, 11556-119 & 11556-122

Hi Doug,

sorry its taken a little while to get back to you about to you about these.

Based on our last call going over the comments here are the conclusions to your concerns:

- you can keep your current language for the pregnant/nursing animals since it is the suggested

- language currently given in the PR notice
- You can keep the brand names/alt brand names the way you have them, however I will put in the amendment letter that the alt. brand name is the only one approved for marketed labels (b/c it specifies "dogs" or "cats" as required)
- You do not need to put "do not allow children to apply" as the KROC statement is enough, however you should add to the storage section "Store out of reach of children and pets" as most all other pesticides (including spot ons) have
- 
- 
- Under "How to Apply" add "Do not have contact or allow children to have contact with treated areas until completely dry." This is consistent with other spot-ons in our branch: 773-93, 773-94, 773-95 & 65331-7 and is consistent with other imidacloprid "homeowner"/consumer products, which have the language "Do not allow children/people or pets to reenter the treated area until dry."
- Under "How to Apply," Where it says "Hold applicator tube in an upright position" revise to say "Hold in in upright position facing away from you and your pet's face and eyes."
- You need add "If Inhaled" to the First Aid box and list it last (per the acute tox memo rating this a category III)

In addition, it appears that per the original tox review the precautionary statements were not correctly added to the label (and overlooked by us too). I will attach the original review below. The memo didn't specifically tell you what to add, only the categories, so based on chapter 7 of the LRM we need to revise the precautionary language to what I have below. (we deleted the long pants/shirt/shoes/glove part)

Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Harmful if swallowed or inhaled. Avoid contact with skin. Wear protective eyewear (goggles, face shield, or safety glasses). Wash hands thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Remove contaminated clothing before reuse. Keep out of reach of children. Do not contaminate food or feed.

(See attached file: 11556-116-122 Acute Toxicity review 3-5-1996.pdf)

Autumn Metzger  
Biologist  
U.S. Environmental Protection Agency  
Insecticide-Rodenticide Branch  
Registration Division (7505P)  
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For alternate languages please go to <http://bayerdisclaimer.bayerweb.com>



Advantage100la.pdf Advantage mitigation response July 3.pdf



RE: 11556-116-122 mitigation amendment comments  
Doug Spilker to: Autumn Metzger

05/16/2012 04:03 PM

History: This message has been replied to.

Hi Autumn,  
I am not available until 1:30 pm your time (12:30 CDT) tomorrow. I eat lunch early so that time would be good, if that's okay with you.

Best Regards,  
Doug

Douglas A. Spilker, Ph.D.  
Manager - EPA Reg. Affairs  
BAYER HEALTHCARE LLC  
Animal Health Division  
Office: 913-268-2751  
Mobile: 816-506-3102  
Email: doug.spilker@bayer.com

Address:  
P.O. Box 390  
Shawnee Mission, KS 66201-0390  
Country: USA

Bayer Animal Health "Protecting.Curing.Caring...Together"

From: Autumn Metzger [mailto:Metzger.Autumn@epamail.epa.gov]  
Sent: Wednesday, May 16, 2012 2:55 PM  
To: Doug Spilker  
Subject: 11556-116-122 mitigation amendment comments

Doug,

I have the comments ready for these. Looks like you missed a bit of what the mitigation asked for and I have other comments to get them up to date. I am in tomorrow and available before 9 am EST and after 11:15 until 3pm. let me know when is good for you. probably 30 min is fine b/c we really only need to do 1 of them and maybe a couple of other comments specific to each size.

thanks,

Autumn Metzger  
Biologist  
U.S. Environmental Protection Agency  
Insecticide-Rodenticide Branch  
Registration Division (7505P)  
1200 Pennsylvania Ave. NW  
Washington, DC 20460

Tel: 703 305-5314



pages (-2) only

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

PESTICIDES AND  
SUBSTANCES

OFFICE OF  
PREVENTION,

TOXIC

3/5/96

**MEMORANDUM**

Subject: I.D. Nos.: 011556-REN 011556-RER, 011556-RRA, 011556-RRI, 011556-RRO,  
011556-RRT. Imidacloprid. Evaluation of Product Labeling Data Submitted and  
Identification of Outstanding Toxicology Data Requirements

Tox. Chem. No. 497E

PC Code No. 129099

DP Barcode Nos. D216769, D216775, D216799, D216803, D216805, D216801

Submission Nos. S489234, S489235, S489237, S489241, S489250, S489251

From: Myron S. Ottley, Ph.D.

Section IV, Toxicology Branch I  
Health Effects Division (7509C)

To: Portia Jenkins/Dennis Edwards, Jr. (PM19)  
Registration Division (7505C)

Through: Marion P. Copley, D.V.M., D.A.B.T.  
Section Head

Review Section IV, Toxicology Branch I  
Health Effects Division (7509C)

**I. CONCLUSIONS**

The existing database supports the following proposed uses for Imidacloprid in the table below. Note the following modifications from the original requests: not for use on 1) kittens, or 2) dogs less than 4 months of age.

→ The 6 acute studies conducted on the formulation (Imidacloprid (Bay T 7491) 10 %) in the above labels are all adequate. This formulation is toxicity category III for acute oral, dermal and inhalation, II for eye irritation, IV for dermal irritation and not a sensitizer.

	Product I.D.	Submission	Formulation	Application
- 119	011556-RRO (Bayer Corp.)	Registration	Advantage 10	For use on dogs 10 lb and under and at least four months old.
- 117	011556-RRT (Bayer Corp.)	Registration	Advantage 20	For use on dogs 11 - 20 lbs. body wt. and at least 4 months old.
- 120	011556-REN (Bayer Corp.)	Registration	Advantage 55	For use on dogs over 20 lbs. body wt. and at least 4 months old.
- 121	011556-RER (Bayer Corp.)	Registration	Advantage 110	For use on dogs over 55 lbs.
- 116	011556-RRA (Bayer Corp.)	Registration	Advantage 9	For use on adule cats 9 lbs. and under.
- 118	0011556-RRI (Bayer Corp.)	Registration	Advantage 18	For use on cats over 9 lbs.

## II. ACTION REQUESTED

TB-1 received for evaluation applications for registration of Advantage 10, Advantage 20, Advantage 55 and Advantage 110 for use on dogs; and Advantage 9 and Advantage 18 for use on cats. TB-1 was asked to evaluate these against the data submitted on the respective imidacloprid formulations to determine if it is adequate to fulfill relevant data requirements. Registration Division has informed TB1 that Imidacloprid formulation Spot On (Imidacloprid 10 %) is the same as Pour On (Imidacloprid 10 %) formulation used in the acutes. All the products identified in the above labels vary only by the size of the single use tubes and the species, age and weight of the animal to be treated.

### III. RESULTS/DISCUSSION

The requirements (CFR 158.135) for uses for Non-Food Uses on pets (for previously registered chemicals) for the Technical and formulation are listed in the following table.

Test	Technical		Formulations§	
	Required	Satisfied	Required	Satisfied
81-1Acute Oral Toxicity	Y	Y	Y	Y
81-2Acute Dermal Toxicity	Y	Y	Y	Y
81-3Acute Inhalation Toxicity	Y	Y	Y	Y
81-4Primary Eye Irritation	Y	Y	Y	Y
81-5Primary Dermal Irritation	Y	Y	Y	Y
81-6Dermal Sensitization	Y	Y	Y	Y
86-1Acute Dermal Toxicity (Cat)	N	-	Y	Y
86-1General Safety Evaluation (Cat)	N	-	Y	Y
86-1Acute Dermal Toxicity (Dog)	N	-	Y	Y
86-1General Safety Evaluation (Dog)	N	-	Y	Y

Y=Yes N=no §Advantage-9, -10, -18, -20, -55, -110 Formulations

#### Data Gaps

The number of kittens tested with Imidacloprid (10 - 11 weeks (MRID 43679502)) was too small. The number of puppies (less than 4 months of age) was also too small (MRID 43679608). Since metabolic pathways are not fully developed in young animals, their toxicity profiles may be different after imidacloprid exposure from the adult animals tested.

As a result, the labels for the imidacloprid formulations should restrict usage of the products to 1) adult cats, and 2) dogs above four months of age. It should be noted that puppies and kittens are considered as separate groups/sex from the adults. The optimum number/sex/age group is six, however 4 is currently being considered minimally adequate until new guidelines are approved. The current studies had only 0-3/sex for puppies (less than 4 months of age) and kittens. In this case, puppies greater than 4 months of age are being considered with the adult groups (this combining is being considered on a case by case basis). Therefore, there are no adequate safety data on 1) kittens, and 2) dogs below the age of 4 months.

The usages/labels covered in this memo should be modified as follows:

Label	Usage (current label)	Restrictions to be added
Advantage 9	For cats and kittens 9 lb and under	Label modification and usage restriction: Not for use on kittens.
Advantage 18	For cats over 9 lb.	None



Label	Usage (current label)	Restrictions to be added
Advantage 10	For small dogs and puppies 10 lbs and under	Label modification and usage restriction: Not for use on puppies under four months.
Advantage 20	For Dogs 11 - 20 lbs	Label modification and usage restriction: Not for use on puppies under four months.
Advantage 55	For dogs over 20 lb	Label modification and usage restriction: Not for use on puppies under four months weeks.
Advantage 110	For dogs over 55 lb	None

No other outstanding data gaps have been identified for these proposed registrations.

### **Margins of Safety**

Dogs and cats were tested at levels up to 50 mg/kg without significant adverse effects. Below is a tabulation of the dose levels expected from exposure to the formulation, and the margins of safety expected at that dose compared with the dose level tested.

# Receipt for Section 3



S 912776

Resubmission: ☐ Yes ☒ No

Regulatory Type: Product Registration - Section 3

Fee For Service: ☐ Yes ☒ No

Application Type: Amendment

Billable: ☐ Yes ☒ No

Company: 11556 BAYER HEALTHCARE LLC

V

Risk Manager: Registration Division, Risk Management Team 1

Product #: 11556-117 Product Name: ADVANTAGE TM 10 (MIDACLOPRID) TOPICAL

Override#:

Me Too

Me Too

Section 3:

Product Name:

Application Date: 01-Mar-2012



OPP Rec'd Date: 05-Mar-2012



Front End Date: 05-Mar-2012



Risk Manager Send Date: 07-Mar-2012



FFS Due Date:

Negotiated Due Date:

OPP Target Date:

Fast Track: ☐

New Ingredient: ☐

Receipt Description:

Label amendment

Form A: ☐

Signature Date:

Form B: ☐

Signature Date:

Print Letter

Enter More Information

Tracking

Receipt Content

Des

Paper Label

View/Edit

New Ingredient

Request Date:

New Ingredient

Received Date:



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

March 7, 2012

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

DR. BRUCE MARTIN  
BAYER HEALTHCARE LLC  
ANIMAL HEALTH DIVISION  
PO Box 390  
SHAWNEE MISSION, KS 66201-0390

PRODUCT NAME: ADVANTAGE TM 10 (IMIDACLOPRID) TOPICAL SOLUTION  
COMPANY NAME: BAYER HEALTHCARE LLC  
OPP IDENTIFICATION NUMBER:  
EPA FILE SYMBOL: 11556-117  
EPA RECEIPT DATE: 03/05/12

SUBJECT: RECEIPT OF AMENDMENT

DEAR REGISTRANT:

The Office of Pesticide Programs has received your application for an amendment and it has passed an administrative screen for completeness.

During the initial screen we determined that the application appears to qualify for fast track review. The package will now be forwarded to the Product Manager for review to determine its acceptability for fast track status.

If you have any questions, please contact Registration Division, Risk Management Team 1, at (703) 308-8045.

Sincerely,

*P. K. Moore*  
Front End Processing Staff  
Information Services Branch  
Information Technology & Resources Management Division

# Fee for Service

{912776H~

This package includes the following

- ☐ New Registration
- ☒ Amendment

- ☐ Studies?      ☐ Fee Waiver?
- ☐ volpay    % Reduction: \_\_\_\_

for Division

- ☐ AD
- ☐ BPPD
- ☒ RD

Risk Mgr. 1

Receipt No.

S-

912776

EPA File Symbol/Reg. No.

11556-117

Pin-Punch Date:

3/5/2012

☒ This item is NOT subject to FFS action.

## Action Code:

Requested:

Granted:

Amount Due: \$ \_\_\_\_

## Parent/Child Decisions:

☒ Inert Cleared for Intended Use


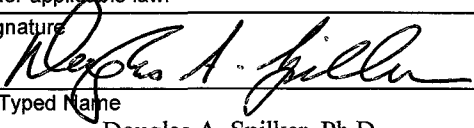


Uncleared Inert in Product

Reviewer: *[Signature]*

Date: 3/7/12

Remarks:

 <b>EPA</b> United States <b>Environmental Protection Agency</b> Washington, DC 20460		<input type="checkbox"/> <b>Registration</b> <input checked="" type="checkbox"/> <b>Amendment</b> <input type="checkbox"/> <b>Other:</b>	OPP Identifier Number
<b>Application for Pesticide - Section I</b>			
1. Company/Product Number <b>11556-117</b>		2. EPA Product Manager <b>Venus Eagle</b>	
4. Company/Product (Name) <b>Advantage 10 Topical Solution</b>		3. Proposed Classification <input checked="" type="checkbox"/> None <input type="checkbox"/> Restricted	
5. Name and Address of Applicant (Include ZIP Code) <b>Bayer HealthCare LLC, Animal Health Division</b> <b>PO Box 390</b> <b>Shawnee Mission, KS 66201</b> <input type="checkbox"/> Check if this is a new address		6. <b>Expedited Review.</b> In accordance with FIFRA Section 3(c)(3) (b)(I), my product is similar or identical in composition and labeling to: EPA Reg. No. _____ Product Name _____	
<b>Section - II</b>			
<input checked="" type="checkbox"/> Amendment – Explain below. <input type="checkbox"/> Final printed labels in response to Agency letter dated _____ <input type="checkbox"/> Resubmission in response to Agency letter dated _____ <input type="checkbox"/> "Me Too" Application <input type="checkbox"/> Notification - Explain below. <input type="checkbox"/> Other - Explain below			
<b>Explanation:</b> <b>NON-PRIA ACTION (AMEND – Pet Spot-on). See attached for more detail.</b> Enclosed for Agency acceptance is revised draft labeling for the subject product, dated 03/01/12. Revisions include those in response to the EPA "Implementation of Label Changes to Pet Spot-On Products" document, dated 9/30/11 (Received 10/11/11), and other minor word and format changes.			
<b>Section - III</b>			
1. Material This Product Will Be Packaged In:			
Child-Resistant Packaging <input type="checkbox"/> Yes* <input type="checkbox"/> No  <b>*Certification must be submitted</b>	Unit Packaging <input type="checkbox"/> Yes <input type="checkbox"/> No If "Yes"                      No. per container Unit Packaging wgt.	Water Soluble Packaging <input type="checkbox"/> Yes <input type="checkbox"/> No If "Yes"                      No. per container Package wgt.	2. Type of Container <input type="checkbox"/> Metal <input type="checkbox"/> Plastic <input type="checkbox"/> Glass <input type="checkbox"/> Paper <input type="checkbox"/> Other (Specify)
3. Location of Net Contents Information <input type="checkbox"/> Label <input type="checkbox"/> Container		4. Size(s) Retail Container	
		5. Location of Label Directions <input type="checkbox"/> On Label <input type="checkbox"/> On labeling accompanying product	
6. Manner in Which Label is Affixed to Product <input type="checkbox"/> Lithograph <input type="checkbox"/> Other _____ <input type="checkbox"/> Paper glued <input type="checkbox"/> Stenciled			
<b>Section - IV</b>			
1. Contact Point (Complete items directly below for identification of individual to be contacted, if necessary, to process this application)			
Name <b>Douglas A. Spilker, Ph.D.</b>		Title <b>Manager, EPA Regulatory Affairs</b>	
		Telephone No. (Include Area Code) <b>913-268-2751</b>	
<b>Certification</b> I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete, and I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.			6. Date Application Received (Stamped)
2. Signature 		3. Title <b>Manager, EPA Regulatory Affairs</b>	
4. Typed Name <b>Douglas A. Spilker, Ph.D.</b> <b>(doug.spilker@bayer.com)</b>		5. Date <b>1 MARCH 2012</b>	

ATTACHMENT FOR  
APPLICATION FOR PESTICIDE REGISTRATION  
March 1, 2012

***Advantage 10 Topical Solution (EPA Reg. No. 11556-117)***

Please find enclosed for the Agency's review and acceptance revised draft labeling, dated 03/01/12, for the subject product. Many of the revisions are in response to the EPA "Implementation of Label Changes to Pet Spot-On Products" document, dated 9/30/11 (Received 10/11/11), but we have also taken the opportunity in this amendment to make a few minor word and format changes. However, there have been no revisions of any efficacy claims.

The proposed changes to the draft labeling are:

**Page 1:**

1. Addition of an Alternate Brand Name to include the word "Dogs," which would be used in any future production of this product. As explained in the cover letter for this action, dated 03/01/12, this product is not currently being produced so no final printed labeling showing this name will be available at this time.
2. Revision of the weight and age restriction statement, with a box surrounding it. The minimum weight was determined from the EPA-accepted Companion Animal Safety studies for this product.
3. Removal of the specific EPA Est. No., as we do not know where this product might be produced in the future.
4. Slight revision of the referral statements.
5. Addition of the "cat prohibition" icon. We do not feel this is necessary since the identical formulation is registered and sold for use on cats. We are acquiescing to the Agency on this point, but ask that this be reconsidered, as it may cause unnecessary worry by the users of the product.

**Page 2:**

5. In the "HAZARDS TO DOMESTIC ANIMALS," addition of the minimum weight for dogs and puppies.
6. Addition of "Side Effects" text in a box; basically the "boiler plate" language specified by the Agency in the aforementioned document, with slight product-specific

modifications, based on the findings in the EPA-accepted Companion Animal Safety studies for this product, and from accident reports from cases of properly applied product.

7. Addition of "DO NOT USE ON CATS" warning box and icon. Again, this should not be necessary since the identical formulation is registered and sold for use on cats. We are acquiescing to the Agency on this point, but ask that this be reconsidered, since it may cause unnecessary worry by the users of the product. Furthermore, we are unaware of any specific data that determined the specific separation period, which we feel is not needed.

**Page 3:**

8. Reformatting of "First Aid" information to be in a box, as required by EPA.
9. Addition of the minimum weight restriction to bullet #1 of the "DIRECTIONS FOR USE."

**Page 4:**

10. Incorporation of the required "do not allow your dog to ingest this product" statement into the language of the bullet #6 of the draft label.
11. Rewording of "GENERAL INFORMATION" to read "PRODUCT INFORMATION" as recommended by the Agency in reviews of other Bayer spot-on products (e.g. K9 Advantix).

**Page 5:**

12. Updating of the headings and reformatting of the "Storage and Disposal" information to be in a box, as required by the Agency.
13. Slight modification of the "Net Contents" statement.

**Page 6:**

- No changes.

No other substantive changes have been made to this label, except for those listed above. Therefore, we hope that these minor changes to the label can be readily accepted by the Agency for this product, as well as, for the revised labels of the four other Advantage dog products – Advantage 20, 55 and 100 Topical Solution - submitted concurrently with this application. **If there are any questions regarding these revisions, please contact us immediately [doug.spilker@bayer.com; (913)-268-2751].**

# Bayer HealthCare

## Animal Health



*Via Federal Express*

March 1, 2012

Document Processing Desk (AMEND- Pet Spot-on)  
Office of Pesticide Programs (7505P)  
U.S. Environmental Protection Agency  
Room S-4900, One Potomac Yard  
2777 South Crystal Drive  
Arlington, VA 22202-4501

Attention: Ms. Venus Eagle/PM 01

Subject: Advantage 10 Topical Solution (EPA Reg. No. 11556-117)  
Advantage 20 Topical Solution (EPA Reg. No. 11556-119)  
Advantage 55 Topical Solution (EPA Reg. No. 11556-120)  
Advantage 100 Topical Solution (EPA Reg. No. 11556-122)

Bayer HealthCare LLC  
Animal Health  
P.O. Box 390  
Shawnee Mission, KS 66201-0390

Dear Ms. Eagle:

Reference is made to the current registrations of the subject products, and the Agency's letter to us, dated September 20, 2011 (received October 11, 2011), regarding "Implementation of Label Changes to Pet Spot-on Products."

Please find enclosed for the Agency's review and acceptance respective applications and revised draft labeling, dated 03/01/12, for each of the subject dog spot-on products. Many of the revisions are in response to the aforementioned EPA "Implementation" letter, but we have also taken the opportunity in these amendments to make a few minor word and format changes. However, there have been no revisions of any efficacy claims.


The letter from the Agency requests the submission of "packaging" of these products. We have replaced these "classic" products in the marketplace with the improved Advantage II products (nee Advantage Plus). We plan to keep the subject "classic" Advantage dog registrations for future use, and therefore we are updating the "Master" labels herein. Since we do not currently market these "classic" products, we do not have Final Printed Labeling (packaging) to submit. We agree to submit updated "packaging" for review before we would ever market these products. This agreement was found acceptable to the Agency in a telephone conversation on Feb. 24, 2012 (K. Nesci with D.A. Spilker).



We will be notifying the Agency in a separate letter that we wish to cancel the registration of **Advantage 110 (EPA Reg. No.11556-121)**, and therefore no revised label for that product is included with this submission.

If you have any questions, please do not hesitate to call (913-268-2751).

Sincerely,



Douglas A. Spilker. Ph. D.

Manager, EPA Regulatory Affairs

[Doug.Spilker.b@Bayer.com](mailto:Doug.Spilker.b@Bayer.com)

Enclosures:

- 1) Advantage 10 - Application w/att.
- 2) Advanatge 10 - Draft label, dated 3/1/12 (3 copies)
- 3) Advantage 20 - Application w/att.
- 4) Advanatge 20 - Draft label, dated 3/1/12 (3 copies)
- 5) Advantage 55 - Application w/att.
- 6) Advantage 55 - Draft label, dated 3/1/12 (3 copies)
- 7) Advantage 100 - Application w/att.
- 8) Advanatge 100 - Draft label, dated 3/1/12 (3 copies)

CC: K. Nesci (EPA)

## Material to be added to an e-Jacket/Jacket

Reg. No. 11SSG-117

Decision # 439552

Description: Accepted Notification (PR 98-10)

1. Placement within the e-Jacket/jacket:

- ☒ Default: (chronological, top = newest)  
☐ File Location: (eg. "before page 45 in .pdf")

2. ☒ Send to Data Extraction contractors this material:

- ☐ Newly stamped accepted label  
☒ Notification  
☐ New CSF  
☐ Other: \_\_\_\_\_

3. Attach this coversheet to the top of the material or jacket. It must be well organized and clipped together, NOT STAPLED. Then give the material with this coversheet to staff in the Information Services Center (Room S-4900).

Reviewer: Jennifer Urzanski  
Phone: 703-347-0156

Division: RD  
Date: 9/13/10



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

SEP 13 2010

Mary McKinney Hunt  
Bayer HealthCare LLC  
Animal Health Division  
PO Box 390  
Shawnee Mission, KS 66201

Subject: Notification of the addition of a Net Contents heading and the optional text [Sample-not for (re)sale] for Advantage® 10 Topical Solution (EPA Reg. # 11556-117)

Dear Ms. McKinney Hunt:

The Agency is in receipt of your Application for Pesticide Notification under Pesticide Registration Notice (PRN) 98-10 dated 8/27/2010 for the product Advantage® 10 Topical Solution (EPA Reg. # 11556-117). The Registration Division (RD) has conducted a review of this request for its applicability under PRN 98-10 and finds that the action(s) requested fall within the scope of PRN 98-10. The Confidential Statement of Formula (CSF) and/or label submitted with the application has (have) been stamped "Notification" and will be placed in our records.

If you have any questions, please call me directly at 703-347-0156 or [urbanski.jennifer@epa.gov](mailto:urbanski.jennifer@epa.gov).

Sincerely,

A handwritten signature in black ink, appearing to read "J. Urbanski".

Jennifer Urbanski  
Registration Division (7505P)  
Office of Pesticide Programs

Note to Reviewer: [Brackets and parentheses indicate alternate language]

**NOTIFICATION**

**SEP 13 2010**

## **Advantage® 10 Topical Solution**

Once-A-Month Topical Flea and Lice Treatment For [Small] Dogs and Puppies 7 Weeks and Older and 10 lbs and Under.

**READ THE ENTIRE LABEL BEFORE EACH USE**

**For the Prevention and Treatment of Flea and Lice Infestations on Dogs**

- One treatment prevents further flea infestation for at least four (4) weeks
- Kills fleas on dogs within 12 hours
- Kills fleas before they lay eggs
- Convenient, easy to apply
- Kills [(biting) (chewing)] lice
- For treatment and prevention of [(biting) (chewing)] lice [infestations]
- Controls existing [(biting) (chewing)] lice infestations
- Dual protection (against fleas and lice)
- Treats, prevents and controls [(biting) (chewing)] lice [infestations]
- Provides effective control of [(biting) (chewing)] lice [infestations]
- Kills [(biting) (chewing)] lice and prevents further infestations
- For treatment and prevention of infestations with [(biting) (chewing)] lice
- Waterproof
- Fragrance free

	<u>% By Weight</u>
Active Ingredient	
Imidacloprid .....	9.1%
Other Ingredients .....	90.9%
Total .....	100.0%

**EPA Reg. No. 11556-117**

**EPA Est. No. 11556-DEU-1**

**KEEP OUT OF REACH OF CHILDREN**

[For Directions For Use, and Storage and Disposal (instructions), see supplemental labeling inside]

## WARNING

See Below for First Aid and Precautionary Statements

### PRECAUTIONARY STATEMENTS

**HAZARDS TO HUMANS:** Causes eye irritation. Harmful if swallowed. Do not get in eyes or on clothing. Avoid contact with skin. Wash hands thoroughly with soap and warm water after handling. Keep out of reach of children. Do not contaminate feed or food.

### HAZARDS TO DOMESTIC ANIMALS

**For external use only.** Do not use on puppies under seven weeks of age. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing animals. Individual sensitivities, while rare, may occur after using ANY pesticide product for pets. If signs persist, or become more severe, consult a veterinarian immediately. If your animal is on medication, consult your veterinarian before using this or any other product. For consumer questions call 1-800-255-6826. For medical emergencies call 1-800-422-9874.

### FIRST AID

Have the product container or label with you when calling a poison control center or doctor, or going for treatment.

**If in eyes:** Hold eye open and rinse slowly and gently with water for 15 – 20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.

**If swallowed:** Call poison control center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by the poison control center or doctor. Do not give anything by mouth to an unconscious person.

**If on skin or clothing:** Take off contaminated clothing. Rinse skin immediately with plenty of water for 15 – 20 minutes. Call a poison control center or doctor for treatment advice.

**To Physician:** Treat the patient symptomatically.

### DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling.

## HOW TO APPLY

1. Use only on dogs. Do not use on other animals.
2. Remove one applicator tube from the package.

[Visuals Depicting How to Open Applicator Tube]

3. Hold applicator tube in an upright position. Pull cap off tube.
4. Turn the cap around and place other end of cap back on tube.
5. Twist cap to break seal, then remove cap from tube.

[Visuals Depicting Application To Animal]

6. The dog should be standing for easy application. Part the hair on the dog's back, between the shoulder blades, until the skin is visible. Place the tip of the tube on the skin and squeeze the tube to *expel the entire contents directly on the skin.*

*Do not get this product in your pet's eyes or mouth.*

7. Discard empty tube as described in Storage and Disposal.
8. In case of severe flea infestation, retreatment may be necessary earlier than four weeks. Do not retreat more often than once every seven days. After flea control is attained, return to a monthly retreatment schedule.

## GENERAL INFORMATION

The successive feeding activity of fleas on pets may elicit a hypersensitivity skin disorder known as flea allergy dermatitis (FAD). Treatment of dogs with Advantage kills fleas and may reduce the incidence of this condition.

Advantage kills fleas on dogs within 12 hours. Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting for up to four (4) weeks. Pre-existing pupae in the environment may continue to emerge for six (6) weeks or longer depending upon the climatic conditions.

Larval flea stages in the pet's surroundings are killed following contact with an Advantage treated pet.

Advantage is waterproof and remains effective following a shampoo treatment, swimming or after exposure to rain or sunlight.

Monthly treatments are required for optimal control and prevention of fleas.

## STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

**Storage:** Store in a cool, dry place.

**Disposal:** Nonrefillable container. **If empty:** Do not reuse or refill this container. Place in trash or offer for recycling if available.

**If partly filled:** Call your local solid waste agency or 1-800-422-9874 for disposal instructions. Never place unused product down any indoor or outdoor drain.

## LIMITED WARRANTY AND LIMITATION OF DAMAGES

Bayer HealthCare LLC, Animal Health Division warrants that this material conforms to the chemical description on the label. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, BAYER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY, INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR MERCHANTABILITY, and no agent of Bayer is authorized to do so except in writing with a specific reference to this warranty. Any damages arising from a breach of this warranty shall be limited to direct damages and shall not include consequential commercial damages such as loss of profits or values, etc.

Net Contents: XX 0.014 fl. oz. (0.4 mL) Tubes

[Sample – Not for (Re)Sale]

Manufactured For  
Bayer HealthCare LLC  
Animal Health Division  
P.O. Box 390  
Shawnee Mission, Kansas 66201 USA

Made in Germany

[Label on Individual Tube]

Advantage® 10

9.1% Imidacloprid

0.014 fl. oz. (0.4 mL)

EPA Reg. No. 11556-117

Warning

Keep Out of Reach of Children

Read The Entire Label Before Use

BAYER

Lot No. 00000000



**EPA**

United States  
**Environmental Protection Agency**  
 Washington, DC 20460

☐ **Registration**  
☐ **Amendment**  
☒ **Other:**

OPP Identifier Number

**Application for Pesticide - Section I**

1. Company/Product Number <b>11556-117</b>	2. EPA Product Manager Venus Eagle	3. Proposed Classification <input checked="" type="checkbox"/> None <input type="checkbox"/> Restricted
4. Company/Product (Name) <b>Advantage 10 Topical Solution</b>	PM# <b>01/Team 1</b>	
5. Name and Address of Applicant (Include ZIP Code) <b>Bayer HealthCare LLC, Animal Health Division PO Box 390 Shawnee Mission, KS 66201</b>	6. <b>Expedited Review.</b> In accordance with FIFRA Section 3(c)(3) (b)(I), my product is similar or identical in composition and labeling to: EPA Reg. No. _____ Product Name _____	
<input type="checkbox"/> Check if this is a new address		

**Section - II**

<input type="checkbox"/> Amendment - Explain below.	<input type="checkbox"/> Final printed labels in response to Agency letter dated _____
<input type="checkbox"/> Resubmission in response to Agency letter dated _____	<input type="checkbox"/> "Me Too" Application
<input checked="" type="checkbox"/> Notification - Explain below.	<input type="checkbox"/> Other - Explain below

**Explanation:** Use additional page(s) if necessary. (For Section I and Section II.)**NOTIFICATION****SEP 13 2010****NON PRIA ACTION.** Please see attached for more detail.

Enclosed for Agency acceptance is a draft label for Advantage 10 Topical Solution (EPA Reg. No. 11556-117). The proposed revisions are the addition of 1) Net Contents heading and 2) optional text: [Sample-not for (re)sale].

**Section - III**

1. Material This Product Will Be Packaged In:				2. Type of Container	
Child-Resistant Packaging <input type="checkbox"/> Yes* <input type="checkbox"/> No	Unit Packaging <input type="checkbox"/> Yes <input type="checkbox"/> No	Water Soluble Packaging <input type="checkbox"/> Yes <input type="checkbox"/> No		<input type="checkbox"/> Metal	
	If "Yes" Unit Packaging wgt.	No. per container	If "Yes" Package wgt.	No. per container	<input type="checkbox"/> Plastic
<b>*Certification must be submitted</b>					<input type="checkbox"/> Glass
					<input type="checkbox"/> Paper
					<input type="checkbox"/> Other (Specify)
3. Location of Net Contents Information <input type="checkbox"/> Label <input type="checkbox"/> Container		4. Size(s) Retail Container		5. Location of Label Directions <input type="checkbox"/> On Label <input type="checkbox"/> On labeling accompanying product	
6. Manner in Which Label is Affixed to Product <input type="checkbox"/> Lithograph <input type="checkbox"/> Paper glued <input type="checkbox"/> Stenciled <input type="checkbox"/> Other _____					

**Section - IV**

1. Contact Point (Complete items directly below for identification of individual to be contacted, if necessary, to process this application).		
Name Mary M. Hunt	Title Pesticide Registrations Manager	Telephone No. (Include Area Code) <b>913-268-2311</b>
<b>Certification</b> I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.		6. Date Application Received (Stamped)    
2. Signature 	3. Title Pesticide Registrations Manager	
4. Typed Name Mary M. Hunt	5. Date <b>8-27-2010</b>	

Enclosed for Agency acceptance is a draft label for Advantage 10 Topical Solution, EPA Reg. No. 11556-117. The proposed revisions are the addition of 1) the "Net Contents" heading and 2) optional text: [Sample-not for (re)sale].

*This notification is consistent with the provisions of PR Notice 98-10 and EPA regulations at 40 CFR 152.46 and no other changes have been made to the labeling or the confidential statement of formula of this product. Bayer understands that it is a violation of 18 U.S.C. Sec. 1001 to willfully make any false statement to EPA. Bayer further understands that if this notification is not consistent with the terms of PR Notice 98-10 and 40 CFR 152.46, this product may be in violation of FIFRA and Bayer may be subject to enforcement action and penalties under sections 12 and 14 of FIFRA.*

[illegible]



# Bayer HealthCare

## Animal Health

August 27, 2010

Document Processing Desk (NOTIF)  
Office of Pesticide Programs (7504P)  
U.S. Environmental Protection Agency  
Room S-4900, One Potomac yard  
2777 South Crystal Drive  
Arlington, VA 22202-4501

Attn: Venus Eagle, PM Team 1

**SUBJECT:** Notification of Label Revision to  
**Advantage® 9 Topical Solution, EPA Reg. No. 11556-116**  
**Advantage® 10 Topical Solution, EPA Reg. No. 11556-118**  
**Advantage® 18 Topical Solution, EPA Reg. No. 11556-117**  
**Advantage® 20 Topical Solution, EPA Reg. No. 11556-119**  
**Advantage® 55 Topical Solution, EPA Reg. No. 11556-120**  
**Advantage® 100 Topical Solution, EPA Reg. No. 11556-122**

Bayer HealthCare LLC  
Animal Health  
P.O. Box 390  
Shawnee Mission, KS 66201

Dear Ms. Eagle:

Please find enclosed for the Agency's acceptance a Notification (EPA Form 8570-1 and attachment) and draft label dated August 27, 2010 for each subject product.

The proposed label revisions are the addition of the "Net Contents" heading and the optional text: [Sample-not for (re)sale].

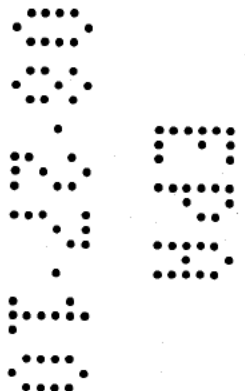
Thank you for your assistance with this notification process, and please contact me at 913-268-2311 or [mary.hunt.b@bayer.com](mailto:mary.hunt.b@bayer.com) if you have any questions or need further information.

Respectfully,

BAYER HEALTHCARE LLC  
ANIMAL HEALTH DIVISION

Mary McKinney Hunt  
Regulatory Specialist

Encl: (6) 8570-1 Application for Pesticide Notification  
(6) Attachment to Application for Pesticide Notification  
(6) Draft Label (3 cc each)  
(6) Highlighted Label (1 cc each)

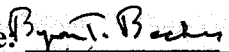



**DATA EVALUATION RECORD FOR  
ENHANCED SPOT-ON REPORTING  
DOG PRODUCT**

**Registration #:** 11556-117, -119, -120, & -122  
**Registrant(s):** Bayer HealthCare LLC  
**Product Name(s):** ADVANTAGE® 10 TOPICAL SOLUTION; ADVANTAGE® 20  
TOPICAL SOLUTION; ADVANTAGE® 55 TOPICAL SOLUTION;  
ADVANTAGE 100® TOPICAL SOLUTION  
**Active Ingredient:** Imidacloprid (9.1%), PC Code: 129099, CAS #138261-41-3

**Application Method:** [11556-117]: ≤10 lbs: Apply contents of one tube (0.4 mL) directly to the skin between the shoulder blades.  
[11556-119]: 11-20 lbs: Apply contents of one tube (1.0 mL) directly to the skin between the shoulder blades.  
[11556-120]: 21-55 lbs: Entire contents of one tube (2.5 mL) should be applied evenly directly to the skin at three or four spots on the top of the back from the shoulder to the base of the tail.  
[11556-122]: >55 lbs: Entire contents of one tube (4.0 mL) should be applied evenly to three or four spots on the top of the back to the base of the tail. At each spot, part the hair until the skin is visible. Place the tip of the tube on the skin and gently squeeze to apply directly to the skin.

**Species:** Puppies (>7 weeks) & Adult Dogs **Weight Ranges:** <10 lbs, 11-20, 21-55, >55 lbs

**Primary Reviewer:** Byron T. Backus, Ph.D. **Signature:**  **Date:** 11/27/09  
**Secondary Reviewer:** Kit Farwell, DVM **Signature:**  **Date:** 11-27-09

**EXECUTIVE SUMMARY:**

**Product:** This report is a review of incident data for EPA Registrations #11556-117, -119, -120 & -122 (Imidacloprid: 9.1%, other ingredients: 90.9%).

**Background:** The data were submitted in response to an Agency request for enhanced reporting of incidents involving topical pet insecticides applied monthly. The Agency request for more data was made at a meeting on May 5, 2009 between EPA, registrants, Canada's Pest Management Regulatory Agency, and other stakeholders. The data are intended to better characterize incidents received in aggregate incident summaries submitted by registrants to the Agency.

The incidents have not been verified and may have causes other than exposure to the pesticide, may be associated with an underlying medical condition, or may be due to misuse of the product (such as overdose, applying on too young an animal, or applying on a different species). The total number of reported incidents may be influenced by many external factors, such as negative

**SEVERITY.** (See Appendix for description of major, moderate, minor).

Most (>97%) of the reported incidents in dogs were minor or moderate (see Tables 1, 2, 3 and 4).

**Table 1. (Reg #11556-117, -119, -120 & -122).**

**Severity: Combined Dermal, Oral and Unknown Routes of Exposure in Dogs, 2008**

Severity*	# of Incidents	Per Cent
Death	4	1.3%
Major	2	0.7%
Moderate	42	13.8%
Minor	256	84.2%
TOTAL	304	

\* See appendix for explanation of severity categories

**Table 2. (Reg #11556-117, -119, -120 & -122).**

**Severity: Dermal Exposure in Dogs\*\*, 2008**

Severity*	# of Incidents	Per Cent
Death	4	1.8%
Major	2	0.9%
Moderate	26	12.0%
Minor	185	85.2%
TOTAL	217	

\* Animals that had both oral and dermal exposures were not included in this table

\*\* See appendix for explanation of severity categories

**Table 3. (Reg #11556-117, -119, -120 & -122).**

**Severity: Unknown Route of Exposure in Dogs, 2008**

Severity*	# of Incidents	Per Cent
Death	0	0.0%
Major	0	0.0%
Moderate	16	18.8%
Minor	69	81.2%
TOTAL	85	

\* See appendix for explanation of severity categories

**Table 7 (Reg #11556-117, -119, -120 & -122).****Severity: Combined (Unknown Route and Dermal) Exposure in Cats, 2008**

Severity*	# of Incidents	Per Cent
Death	3	1.3%
Major	0	0.0%
Moderate	29	12.6%
Minor	198	86.1%
TOTAL	230	100.00

\* See appendix for explanation of severity categories

There are no records of oral exposure in cats from use of these products,

**GENDER**

For dogs, males and females are about equally represented in the incident reports (see Table 8).

**Table 8 (Reg #11556-117, -119, -120 & -122).****Gender: Dermal Exposure in Dogs, 2008**

Sex	# of Incidents	Per Cent
Female	112	52.1%
Male	103	47.9%
TOTAL	215	

**Note:** Gender was not reported for all incidents.

**Table 10. (Reg ##11556-117, -119, -120 & -122)****Body Weight: Dermal Exposure in Dogs, 2008. # of Incidents (%)**

<b>Severity*</b> <b>Body Wt</b> <b>(pounds)</b>	<b>Death</b>	<b>Major</b>	<b>Moderate</b>	<b>Minor</b>	<b>Total</b>	<b>%</b>
< 5	2 (1)	0	5 (3)	8 (4)	15	8
> 5 – 11	0	0	2 (1)	30 (16)	32	16
11 – 21	0	0	6 (3)	50 (25)	56	28
21 – 31	0	1 (<1)	3 (2)	19 (10)	23	12
31 – 41	1 (<1)	0	1 (<1)	11 (6)	13	7
41 – 51	0	0	2 (1)	13 (7)	15	8
51 – 61	0	0	1 (<1)	16 (8)	17	9
≥61	1 (<1)	0	3 (2)	24 (12)	28	14
<b>TOTAL</b>	<b>4 (2)</b>	<b>1 (&lt;1)</b>	<b>23 (12)</b>	<b>171 (87)</b>	<b>199</b>	

**Note:** Not all body weights were reported.

Weight range (x – y) indicates weight from x up to but not including y

\* Severity key (See appendix for explanation of severity categories)

As can be seen in table 11, there were 37 reported incidents in which the dog weight was below the range specified by the product, indicating misuse.

**Table 11. (Reg #11556-117, -119, -120 & -122)****Product Weight Range: Dermal Exposure in Dogs, 2008**

<b>Dog wt. vs. Product wt. range</b>	<b># Incidents</b>	<b>Per Cent</b>
Dog weight < product weight range*	37	22.70
<b>TOTAL incidents</b>	<b>163</b>	

\*This table indicates product misuse and is a summary of all product use weight ranges

NOTE: not all body weights or product used were reported



**SYSTEMS and CLINICAL SIGNS**

As can be seen in Table 13, many of the symptoms observed were dermal and involved the application site (pruritus, scratching, alopecia), but some were digestive (diarrhea), behavioral (hyperactivity, agitation), or systemic (lethargy). Salivation or drooling (and possibly even the hyperactivity and agitation) may result from the very bitter taste of imidacloprid (<http://www.pet-care-experts.com/archive.php?2003052509592627>). There were also a few occurrences of facial edema.

**Table 13. (Reg #11556-117, -119, -120 & -122)  
Clinical Signs: Dermal Exposure in Dogs, 2008.**

Symptoms - short description	Count Of Symptoms (%)
Dermal	132 (26)
Digestive	61 (12)
Behavioral	58 (11)
Systemic Disorders	52 (10)
General Signs	50 (10)
Neurological	50 (10)
Lethargy	34 (7)
Immune System	20 (4)
Salivation	19 (4)
Eye	13 (3)
Respiratory	11 (2)
Death	4 (<1)
Convulsions	4 (<1)
Paralysis	3 (<1)
Ear	2 (<1)
Musculoskeletal	1 (<1)
Renal	1 (<1)
Hepatic	1 (<1)
Total	516

**BRIEF SUMMARY OF TOXICITY:****Active ingredient:**

Imidacloprid is a member of the pyridylmethylaniline class of compounds. Its mode of action is the disruption of the nervous system by acting as an inhibitor at nicotinic acetylcholine receptors. Imidacloprid blocks the signals that are induced by acetylcholine at the post-synaptic membrane, resulting in normal nerve function impairment.

Different mammalian species have varying susceptibilities to imidacloprid as the mouse has an oral LD<sub>50</sub> (see <http://pmep.cce.cornell.edu/profiles/extoxnet/haloxypop->



rate (2.0 mL if < 10 lbs; 5.0 mL if > 10 lbs) at weekly intervals for eight treatments. Six puppies/sex were treated with the vehicle control at the recommended use rate (0.4 mL if < 10 lbs; 1.0 mL if > 10 lbs) at weekly intervals for eight treatments. There was no evidence of treatment-related toxicity in clinical signs or clinical pathology parameters. All animals gained weight during the study. It was demonstrated that 7 week-old puppies can tolerate a dose of 5X the recommended use rate. The study is considered acceptable and satisfies the draft guideline requirements (81-6) for a domestic animal safety study. Note that the puppies treated with the vehicle control were given a 1X dose level; there is a solvent in this formulation that may be toxic to younger animals if ingested; the bitter taste of the imidacloprid may discourage the puppies from grooming themselves.

The acute oral toxicity study used to support the registrations of these products is in MRID 43679601. Groups of 6M and 6F young adult (8-10 weeks old) Sprague-Dawley rats received single oral doses of Imidacloprid 10% at 495, 1020, 1430, 1910 or 2620 mg/kg with 14-day observation. Treatment-related clinical signs including hypoactivity, clonic convulsions, labored breathing and oral staining were observed at all dose levels. Treatment-related necropsy findings were observed in decedents and included nasal staining, red fluid in bladder, bilaterally reddened lungs and reddened mucosae. The oral LD<sub>50</sub> (males) = 1943 mg/kg (95% C.I. not calculable), for females = 1732 mg/kg (95% C.I. 1416-2147 mg/kg); combined sexes = 1838 mg/kg (95% C.I. not calculable).

The acute dermal toxicity study used to support the registrations of these products is in MRID 43679602. There were no deaths at 2000 mg/kg (=Toxicity Category III).

The signal word for this formulation is WARNING, based on the eye irritation study (one of 6 rabbits had corneal opacity on day 7) and one of 6 had iritis on day 7 (not known whether this was the same rabbit with corneal opacity).

According to TXR 009960 the acute oral LD<sub>50</sub> of technical (94%) imidacloprid is 424 mg/kg in male rats and >450 but <475 mg/kg in female rats (from the study in MRID 42055331). Based on these values, and assuming the additional ingredients are toxicologically inert, a 10% imidacloprid formulation would have an oral LD<sub>50</sub> in male rats of 3986 [9.4 x 424] mg/kg and 4348 [9.4 x 462] mg/kg in females, although other factors (such as solubility considerations and bioavailability) could modify these calculated values.

#### **Information from NPIC:**

There is one incident in the NPIC Spot-On Reports for 2009 for Advantage Green, identified as containing 10.0% imidacloprid. Advantage Green is apparently for dogs weighing less than 10 lbs (which would correspond to 11556-117). The incident involved a neutered male 8 year-old Papillon weighing 1.2 kg (2.7 lbs). According to the DVM's note: "I am unsure that this case is related to a reaction to Advantage, but the dog's owner is convinced that it is and requested an adverse reaction report be submitted. Dog had a normal physical examination the week prior to this occurring. No history of cardiac disease. I think it likely that there was another cause but no necropsy was performed."

## APPENDIX

### EXPOSURE TYPE AND SEVERITY CATEGORIES

Excerpted From Pesticide Registration Notice 98-3, April 3, 1998.

#### ***D-A - Domestic Animal Death***

§159.184 (5)(ii)(A): "If the domestic animal died or was euthanized."

It was reported that the animal died or was euthanized as a result of exposure or as a direct complication of exposure to the pesticide.

#### ***D-B - Domestic Animal Major***

§159.184 (5)(ii)(B): "If the domestic animal exhibited or was alleged to have exhibited symptoms which may have been life-threatening or resulted in residual disability."

Life-threatening effects include, but are not limited to, massive or internal hemorrhage, loss of consciousness, grand mal seizures, paralysis, cardio-respiratory depression and bronchoconstriction requiring immediate treatment. In general, life-threatening effects are any condition which, if untreated, would likely lead to death. Residual disability includes adverse effects which last for an extended period of time after the initial poisoning and may affect the life span for the animal. An example of an adverse effect which may last for an extended period of time is the case of a cat that developed severe weakness lasting for weeks to months after organophosphate exposure. An example of a residual disability that may affect the life span of an animal is the case of a dog which recovered from cholecalciferol rodenticide ingestion but is left with decreased renal function.

#### ***D-C - Domestic Animal Moderate***

§159.184 (5)(ii)(C): "If the domestic animal exhibited or was alleged to have exhibited symptoms which are more pronounced, more prolonged or a more systemic nature than minor symptoms. Usually some form of treatment would have been indicated to treat the animal. Symptoms were not life-threatening and the animal has returned to its pre-exposure state of health with no additional residual disability."

Effects include, but are not limited to, corneal abrasion, difficulty breathing, hyperthermia, isolated focal seizures, gastrointestinal symptoms leading to dehydration, caustic injury to mouth or esophagus, severe muscle weakness, incoordination, tremors and hives. More prolonged effects are those that last one month or longer, such as a persistent skin rash.

#### ***D-D - Domestic Animal Minor***

§159.184 (5)(ii)(D): "If the domestic animal was alleged to have exhibited symptoms, but they were minimally bothersome. The symptoms resolved rapidly and usually involved skin, eye or respiratory irritation."

Effects include, but are not limited to, excessive salivation, skin rash, itching, conjunctivitis, lethargy, transient cough, mild gastrointestinal symptoms of a short duration and minor behavioral changes such as agitation and hyperactivity.

## Material to be added to an e-Jacket/Jacket

Reg. No. 11556-117 Decision #                     

Description: Notification per PRN 98-10

\_\_\_\_\_

1. Placement within the e-Jacket/jacket:

- ☐ Default: (chronological, top = newest)
  - ☐ File Location: (eg. "before page 45 in .pdf")
- \_\_\_\_\_

2. ☒ Send to Data Extraction contractors this material:

- ☐ Newly stamped accepted label
- ☒ Notification
- ☐ New CSF
- ☐ Other: \_\_\_\_\_

3. Attach this coversheet to the top of the material or jacket. It must be well organized and clipped together, NOT STAPLED. Then give the material with this coversheet to staff in the Information Services Center (Room S-4900).

Reviewer: Julie Chao

Phone: 703-308-8735

Division: RD/IRB

Date: 1-7-09

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460



OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

January 7, 2010

Douglas A. Spilker  
Bayer HealthCare, LLC  
Animal Health Division  
P.O. Box 390  
Shawnee Mission, KS 66201-0390

Dear Dr. Spilker,

Subject: Label Notifications per Pesticide Registration Notice 98-10

The Agency is in receipt of your Applications for Pesticide Notification under Pesticide Registration Notice (PRN) 98-10, dated December 7, 2009, for the following products:

- Advantage 9 Topical Solution, EPA Registration Number 11556-116
- Advantage 10 Topical Solution, EPA Registration Number 11556-117
- Advantage 18 Topical Solution, EPA Registration Number 11556-118
- Advantage 20 Topical Solution, EPA Registration Number 11556-119
- Advantage 55 Topical Solution, EPA Registration Number 11556-120
- Advantage 100 Topical Solution, EPA Registration Number 11556-122

The Registration Division has conducted a review of these requests for their applicability under PRN 98-10, and finds that the actions requested fall within the scope of PRN 98-10. The information submitted with the applications has been stamped "Notification" and will be placed in our records. If you have any questions, please contact me directly at 703-308-8735 or email me at [chao.julie@epa.gov](mailto:chao.julie@epa.gov).

Sincerely,

A handwritten signature in cursive script, reading "Julie A. Chao".

Julie A. Chao  
Insecticide-Rodenticide Branch  
Registration Division (7505P)  
Office of Pesticide Programs



United States  
Environmental Protection Agency  
Washington, DC 20460

☐ Registration  
☐ Amendment  
☒ Other

OPP Identifier Number

## Application for Pesticide - Section I

1. Company/Product Number 11556-117	2. EPA Product Manager Venus Eagle	3. Proposed Classification <input checked="" type="checkbox"/> None <input type="checkbox"/> Restricted
4. Company/Product (Name) Advantage 10 Topical Solution	PM# 01	
5. Name and Address of Applicant (Include ZIP Code) Bayer HealthCare LLC, Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390 <input type="checkbox"/> Check if this is a new address	6. Expedited Review. In accordance with FIFRA Section 3(c)(3) (b)(i), my product is similar or identical in composition and labeling to: <input checked="" type="checkbox"/> EPA Reg. No. _____ Product Name _____	

## Section - II

<input type="checkbox"/> Amendment - Explain below.	<input type="checkbox"/> Final printed labels in response to Agency letter dated _____
<input type="checkbox"/> Resubmission in response to Agency letter dated _____	<input type="checkbox"/> "Me Too" Application.
<input checked="" type="checkbox"/> Notification - Explain below.	<input type="checkbox"/> Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

NOTIFICATION

See attachment (1p.) for more information.  
Contact: doug.spilker.b@bayer.com

JAN - 7 2010

## Section - III

1. Material This Product Will Be Packaged In:				2. Type of Container	
Child-Resistant Packaging <input type="checkbox"/> Yes* <input checked="" type="checkbox"/> No	Unit Packaging <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Water Soluble Packaging <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No		<input checked="" type="checkbox"/> Metal	
				<input checked="" type="checkbox"/> Plastic	
				<input type="checkbox"/> Glass	
				<input checked="" type="checkbox"/> Paper	
				Other (Specify) _____	
* Certification must be submitted		If "Yes" Unit Packaging wgt.	No. per container	If "Yes" Package wgt.	No. per container
3. Location of Net Contents Information <input checked="" type="checkbox"/> Label <input type="checkbox"/> Container		4. Size(s) Retail Container 1/4/6-0.4mL tbe		5. Location of Label Directions <input type="checkbox"/> On Label <input checked="" type="checkbox"/> On Labeling accompanying product	
6. Manner in Which Label is Affixed to Product <input checked="" type="checkbox"/> Lithograph <input type="checkbox"/> Paper glued <input type="checkbox"/> Stenciled		<input type="checkbox"/> Other _____			

## Section - IV

1. Contact Point (Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)		
Name Douglas A. Spilker, Ph.D.	Title Manager, EPA Reg. Affairs	Telephone No. (Include Area Code) 913-268-2751
<b>Certification</b> I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.		6. Date Application Received (Stamped)
2. Signature 	3. Title Manager, EPA Reg. Affairs	
4. Typed Name Douglas A. Spilker, Ph.D.	5. Date 7 Dec 2009	

### Section II – Explanation:

We are also notifying the Agency, pursuant to PR Notice 98-10, that we will be adding the following optional text to final printed labeling of the appropriate size product, as needed:

["Sample – Not for Resale"]

*This notification is consistent with the provisions of PR Notice 98-10 and EPA regulations at 40 CFR 152.46 and no other changes have been proposed for the labeling or the confidential statement of formula for this product. Bayer understands that it is a violation of 18 U.S. C. Sec. 1001 to willfully make any false statement to EPA. Bayer further understands that if this notification is not consistent with the terms of PR Notice 98-10 and 40 CFR 152.46, this product may be in violation of FIFRA and Bayer may be subject to enforcement action and penalties under sections 12 and 14 of FIFRA.*

[illegible]

Reason To Issue: Show additional package size.

Date: 01/05/10

Supersedes: 09/05/08

**NOTIFICATION**

Note to Reviewer: [Brackets and parentheses indicate alternate language]

**JAN - 7 2010**

**Advantage® 10 Topical Solution**

Once-A-Month Topical Flea and Lice Treatment For [Small] Dogs and  
Puppies 7 Weeks and Older and 10 lbs and Under.

**READ THE ENTIRE LABEL BEFORE EACH USE**

For the Prevention and Treatment of Flea and Lice Infestations on Dogs

- One treatment prevents further flea infestation for at least four (4) weeks
- Kills fleas on dogs within 12 hours
- Kills fleas before they lay eggs
- Convenient, easy to apply
- Kills [(biting) (chewing)] lice
- For treatment and prevention of [(biting) (chewing)] lice [infestations]
- Controls existing [(biting) (chewing)] lice infestations
- Dual protection (against fleas and lice)
- Treats, prevents and controls [(biting) (chewing)] lice [infestations]
- Provides effective control of [(biting) (chewing)] lice [infestations]
- Kills [(biting) (chewing)] lice and prevents further infestations
- For treatment and prevention of infestations with [(biting) (chewing)] lice
- Waterproof
- Fragrance free

	<u>% By Weight</u>
Active Ingredient	
Imidacloprid .....	9.1%
Other Ingredients .....	90.9%
Total .....	100.0%

**EPA Reg. No. 11556-117**

**EPA Est. No. 11556-DEU-1**

**KEEP OUT OF REACH OF CHILDREN**

[For Directions For Use, and Storage and Disposal (instructions),  
see supplemental labeling inside]

Reason To Issue: Show additional package size.

Date: 01/05/10

Supersedes: 09/05/08

---

### WARNING

See Below for First Aid and Precautionary Statements

#### PRECAUTIONARY STATEMENTS

**HAZARDS TO HUMANS:** Causes eye irritation. Harmful if swallowed. Do not get in eyes or on clothing. Avoid contact with skin. Wash hands thoroughly with soap and warm water after handling. Keep out of reach of children. Do not contaminate feed or food.

#### HAZARDS TO DOMESTIC ANIMALS

**For external use only.** Do not use on puppies under seven weeks of age. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing animals. Individual sensitivities, while rare, may occur after using ANY pesticide product for pets. If signs persist, or become more severe, consult a veterinarian immediately. If your animal is on medication, consult your veterinarian before using this or any other product. For consumer questions call 1-800-255-6826. For medical emergencies call 1-800-422-9874.

#### FIRST AID

Have the product container or label with you when calling a poison control center or doctor, or going for treatment.

**If in eyes:** Hold eye open and rinse slowly and gently with water for 15 – 20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.

**If swallowed:** Call poison control center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by the poison control center or doctor. Do not give anything by mouth to an unconscious person.

**If on skin or clothing:** Take off contaminated clothing. Rinse skin immediately with plenty of water for 15 – 20 minutes. Call a poison control center or doctor for treatment advice.

**To Physician:** Treat the patient symptomatically.

#### DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling.



Reason To Issue: Show additional package size.

Date: 01/05/10

Supersedes: 09/05/08

---

## HOW TO APPLY

1. Use only on dogs. Do not use on other animals.
2. Remove one applicator tube from the package.

[Visuals Depicting How to Open Applicator Tube]

3. Hold applicator tube in an upright position. Pull cap off tube.
4. Turn the cap around and place other end of cap back on tube.
5. Twist cap to break seal, then remove cap from tube.

[Visuals Depicting Application To Animal]

6. The dog should be standing for easy application. Part the hair on the dog's back, between the shoulder blades, until the skin is visible. Place the tip of the tube on the skin and squeeze the tube to *expel the entire contents directly on the skin.*

*Do not get this product in your pet's eyes or mouth.*

7. Discard empty tube as described in Storage and Disposal.
8. In case of severe flea infestation, retreatment may be necessary earlier than four weeks. Do not retreat more often than once every seven days. After flea control is attained, return to a monthly retreatment schedule.

## GENERAL INFORMATION

The successive feeding activity of fleas on pets may elicit a hypersensitivity skin disorder known as flea allergy dermatitis (FAD). Treatment of dogs with Advantage kills fleas and may reduce the incidence of this condition.

Advantage kills fleas on dogs within 12 hours. Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting for up to four (4) weeks. Pre-existing pupae in the environment may continue to emerge for six (6) weeks or longer depending upon the climatic conditions.

Reason To Issue: Show additional package size.

Date: 01/05/10

Supersedes: 09/05/08

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Larval flea stages in the pet's surroundings are killed following contact with an Advantage treated pet.

Advantage is waterproof and remains effective following a shampoo treatment, swimming or after exposure to rain or sunlight.

Monthly treatments are required for optimal control and prevention of fleas.

#### **STORAGE AND DISPOSAL**

Do not contaminate water, food or feed by storage or disposal.

**Storage:** Store in a cool, dry place.

**Disposal:** Nonrefillable container. **If empty:** Do not reuse or refill this container. Place in trash or offer for recycling if available.

**If partly filled:** Call your local solid waste agency or 1-800-422-9874 for disposal instructions. Never place unused product down any indoor or outdoor drain.

#### **LIMITED WARRANTY AND LIMITATION OF DAMAGES**

Bayer HealthCare LLC, Animal Health Division warrants that this material conforms to the chemical description on the label. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, BAYER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY, INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR MERCHANTABILITY, and no agent of Bayer is authorized to do so except in writing with a specific reference to this warranty. Any damages arising from a breach of this warranty shall be limited to direct damages and shall not include consequential commercial damages such as loss of profits or values, etc.

[One] [Four] [Six] 0.014 fl. oz. (0.4 mL) Tubes

**OPTIONAL CLAIM FOR THE ONE TUBE PACKAGE:** [Sample – Not for (Re)Sale]

Manufactured For

Bayer HealthCare LLC

Animal Health Division

P.O. Box 390

Shawnee Mission, Kansas 66201 USA

Made in Germany

Reason To Issue: Show additional package size.

Date: 01/05/10

Supersedes: 09/05/08

---

[Label on Individual Tube]

Advantage® 10

9.1% Imidacloprid

0.014 fl. oz. (0.4 mL)

EPA Reg. No. 11556-117

Warning

Keep Out of Reach of Children

Read The Entire Label Before Use

BAYER

Lot No. 0000000



United States  
Environmental Protection Agency  
Washington, DC 20460

☐ Registration  
☐ Amendment  
☒ Other

OPP Identifier Number

## Application for Pesticide - Section I

1. Company/Product Number 11556-117	2. EPA Product Manager Venus Eagle	3. Proposed Classification <input checked="" type="checkbox"/> None <input type="checkbox"/> Restricted
4. Company/Product (Name) Advantage 10 Topical Solution	PM# 01	
5. Name and Address of Applicant (Include ZIP Code) Bayer HealthCare LLC, Animal Health Division PO Box 390 Shawnee Mission, KS 66201-0390 <input type="checkbox"/> Check if this is a new address	6. Expedited Review. In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to: <input checked="" type="checkbox"/> EPA Reg. No. _____ Product Name _____	

## Section - II

<input type="checkbox"/> Amendment - Explain below.	<input checked="" type="checkbox"/> Final printed labels in response to Agency letter dated Nov. 4, 2008
<input type="checkbox"/> Resubmission in response to Agency letter dated _____	<input type="checkbox"/> "Me Too" Application.
<input type="checkbox"/> Notification - Explain below.	<input type="checkbox"/> Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

## Section - III

1. Material This Product Will Be Packaged In:				2. Type of Container	
Child-Resistant Packaging <input type="checkbox"/> Yes* <input type="checkbox"/> No	Unit Packaging <input type="checkbox"/> Yes <input type="checkbox"/> No	Water Soluble Packaging <input type="checkbox"/> Yes <input type="checkbox"/> No		<input type="checkbox"/> Metal	
				<input type="checkbox"/> Plastic	
				<input type="checkbox"/> Glass	
				<input type="checkbox"/> Paper	
				<input type="checkbox"/> Other (Specify) _____	
* Certification must be submitted		If "Yes" Unit Packaging wgt.	No. per container	If "Yes" Package wgt	No. per container
3. Location of Net Contents Information <input type="checkbox"/> Label <input type="checkbox"/> Container		4. Size(s) Retail Container		5. Location of Label Directions <input type="checkbox"/> On Label <input type="checkbox"/> On Labeling accompanying product	
6. Manner in Which Label is Affixed to Product <input type="checkbox"/> Lithograph <input type="checkbox"/> Paper glued <input type="checkbox"/> Stenciled		<input type="checkbox"/> Other _____			

## Section - IV

1. Contact Point (Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)			
Name Douglas A. Spilker, Ph.D.		Title Manager, EPA Reg. Affairs	
		Telephone No. (Include Area Code) 913-268-2757	
Certification I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.			6. Date Application Received (Stamped)
2. Signature 		3. Title Manager, EPA Reg. Affairs	
4. Typed Name Douglas A. Spilker, Ph.D.		5. Date 12 Feb 2009	

OT REVIEWED  
ce with PR Notice 82-2  
Based on Draft Labeling Dated

Topical Solution

10 advantage 10  
Based on Draft Labeling Dated

advantage 10  
Topical Solution

7 Weeks and Older  
and 10 lbs. and Under

6 Pack

16x25x16

10 lbs.  
and  
Under



advantage 10

Topical Solution

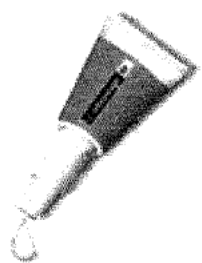
Once-a-Month Topical Flea and Lice Treatment  
for Dogs and Puppies 7 Weeks and Older  
and 10 lbs. and Under






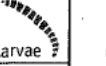


- Kills fleas on dogs within 12 hours
- Kills fleas before they lay eggs
- Convenient, easy to apply

Active Ingredient	% By Weight
Imidacloprid.....	9.1 %
Other Ingredients.....	90.9 %
Total .....	100.0 %

6 Pack  
KEEP OUT OF REACH  
OF CHILDREN  
WARNING

See back panel for First Aid.  
For Directions for Use, and Storage and  
Disposal, see supplemental labeling inside.



 Waterproof	 Waterproof
 Fleas	 Fleas
 Flea Larvae	 Flea Larvae
 Lice	 Lice
6 Pack	6 Pack

advantage 10  
Topical Solution

advantage 10  
Topical Solution

Once-a-Month Topical Flea and Lice Treatment  
for Dogs and Puppies 7 Weeks and Older  
and 10 lbs. and Under

READ THE ENTIRE LABEL BEFORE EACH USE

For the Prevention and Treatment of  
Flea and Lice Infestations on Dogs  
• Kills fleas on dogs within 12 hours  
• Kills fleas before they lay eggs

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS:  
Causes eye irritation. Harmful if swallowed.  
Do not get in eyes or on clothing. Avoid contact  
with skin. Wash hands thoroughly with soap and  
warm water after handling. Keep out of reach of  
children. Do not contaminate feed or food.

HAZARDS TO DOMESTIC ANIMALS  
For external use only. Do not use on puppies  
under seven weeks of age. As with any product,  
consult your veterinarian before using this  
product on debilitated, aged, pregnant or nursing  
animals. Individual sensitivities, while rare, may  
occur after using ANY pesticide product for pets.  
If signs persist, or become more severe, consult a  
veterinarian immediately. If your animal is on  
medication, consult your veterinarian before  
using this or any other product.

For consumer questions call 1-800-255-6826.  
For medical emergencies call 1-800-422-9874.

FIRST AID

Have the product container or label with you  
when calling a poison control center or doctor,  
or going for treatment.

If in eyes:

Hold eye open and rinse slowly and gently  
with water for 15-20 minutes.  
Remove contact lenses, if present, after the  
first 5 minutes, then continue rinsing eye.  
Call a poison control center or doctor for  
treatment advice.

Manufactured for Bayer HealthCare LLC,  
Animal Health Division, P.O. Box 390,  
Shawnee Mission, KS, 66201, USA  
Bayer, the Bayer Cross and Advantage  
are registered trademarks of Bayer.

Made in Germany  
© 2009 Bayer HealthCare LLC

If swallowed:

Call poison control center or doctor immediately  
for treatment advice. Have person sip a glass of  
water if able to swallow. Do not induce vomiting  
unless told to do so by the poison control center  
or doctor. Do not give anything by mouth to an  
unconscious person.

If on skin or clothing:

Take off contaminated clothing. Rinse skin  
immediately with plenty of water for 15-20  
minutes. Call a poison control center or doctor for  
treatment advice.

To Physician: Treat the patient symptomatically.

DIRECTIONS FOR USE

It is a violation of Federal Law to use this product  
in a manner inconsistent with its labeling.

HOW TO APPLY

1. Use only on dogs. Do not use on other animals.
2. Remove one applicator tube from the package.
3. Hold applicator tube in an upright position.  
Pull cap off tube.
4. Turn the cap around and place other end of cap  
back on tube.
5. Twist cap to break seal, then remove cap from  
tube.



6. The dog should be standing for easy  
application. Part the hair on the dog's back,  
between the shoulder blades, until the skin is  
visible. Place the tip of the tube on the skin and  
squeeze the tube to expel the entire contents  
directly on the skin.  
Do not get this product in your pet's eyes or  
mouth.

7. Discard empty tube as described in Storage  
and Disposal.

8. In case of severe flea infestation, retreatment  
may be necessary earlier than four weeks.  
Do not retreat more often than once every  
seven days. After flea control is attained, return  
to a monthly retreatment schedule.

01791706-053899, R.6  
EPA Est. No. 11556 DEU-1  
EPA Reg. No. 11556-117

Bayer HealthCare

Lot No.:





# advantage<sup>®</sup> 10

## Topical Solution

### Once-A-Month Topical Flea and Lice Treatment for Dogs and Puppies 7 Weeks and Older and 10 lbs. and Under

#### READ THE ENTIRE LABEL BEFORE EACH USE.

For the Prevention and Treatment of Flea and Lice Infestations on Dogs

One treatment prevents further flea infestation for at least four weeks

Kills fleas on dogs within 12 hours

Kills fleas before they lay eggs

Waterproof

Fragrance-free

#### Active Ingredient

Imidacloprid..... 9.1%

Other Ingredients..... 90.9%

Total..... 100.0%

## KEEP OUT OF REACH OF CHILDREN WARNING

See below for First Aid and Precautionary Statements.

#### PRECAUTIONARY STATEMENTS

**HAZARDS TO HUMANS:** Causes eye irritation.

Harmful if swallowed. Do not get in eyes or on clothing.

Avoid contact with skin. Wash hands thoroughly with soap

and warm water after handling. Keep out of reach of children.

Do not contaminate feed or food.

#### HAZARDS TO DOMESTIC ANIMALS

For external use only. Do not use on puppies under seven

weeks of age. As with any product, consult your veterinarian

before using this product on debilitated, aged, pregnant or

nursing animals. Individual sensitivities, while rare, may occur

after using ANY pesticide product for pets.

If signs persist, or become more severe, consult a veterinarian

immediately. If your animal is on medication, consult your

veterinarian before using this or any other product.

For consumer questions call 1-800-255-6826.

For medical emergencies call 1-800-422-9874.

#### FIRST AID

Have the product container or label with you when calling a

poison control center or doctor, or going for treatment.

**If in eyes:** Hold eye open and rinse slowly and gently with

water for 15-20 minutes. Remove contact lenses, if present,

after the first 5 minutes, then continue rinsing eye.

Call a poison control center or doctor for treatment advice.

**If swallowed:** Call poison control center or doctor immediately

for treatment advice. Have person sip a glass of water if able

to swallow. Do not induce vomiting unless told to do so by the

poison control center or doctor. Do not give anything by mouth

to an unconscious person.

**If on skin or clothing:** Take off contaminated clothing.

Rinse skin immediately with plenty of water for 15-20 minutes.

Call a poison control center or doctor for treatment advice.

**To Physician:** Treat the patient symptomatically.

#### DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner

inconsistent with its labeling.

#### HOW TO APPLY

1. Use only on dogs. Do not use on other animals.

2. Remove one applicator tube from the package.

3. Hold applicator tube in an upright position. Pull cap off tube.



4. Turn the cap around and place other end of cap back on tube.

5. Twist cap to break seal, then remove cap from tube.



6. The dog should be standing for easy application. Part the

hair on the dog's back, between the shoulder blades, until the

skin is visible. Place the tip of the tube on the skin and squeeze

the tube to expel the entire contents directly on the skin.

Do not get this product in your pet's eyes or mouth.

7. Discard empty tube as described in Storage and Disposal.

8. In case of severe flea infestation, retreatment may be

necessary earlier than four weeks. Do not retreat more often

than once every seven days. After flea control is attained,

return to a monthly retreatment schedule.

#### GENERAL INFORMATION

The successive feeding activity of fleas on pets may elicit a

hypersensitivity skin disorder known as flea allergy dermatitis

(FAD). Treatment of dogs with Advantage<sup>®</sup> kills fleas and may

reduce the incidence of this condition.

Advantage kills fleas on dogs within 12 hours.

Reinfesting fleas are killed within 2 hours with protection

against further flea infestation lasting for up to four (4) weeks.

Pre-existing pupae in the environment may continue

to emerge for six (6) weeks or longer depending upon the

climatic conditions. Larval flea stages in the pet's surroundings

are killed following contact with an Advantage treated pet.

Advantage is waterproof and remains effective following a

shampoo treatment, swimming or after exposure to rain or

sunlight. Monthly treatments are required for optimal control

and prevention of fleas.

#### STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

**Storage:** Store in a cool, dry place.

**Disposal:** Nonrefillable container.

**If empty:** Do not reuse or refill this container. Place in trash or

offer for recycling if available.

**If partly filled:** Call your local solid waste agency or

1-800-422-9874 for disposal instructions.

Never place unused product down any indoor or outdoor drain.

#### LIMITED WARRANTY AND LIMITATION OF DAMAGES

Bayer HealthCare LLC, Animal Health Division warrants that

this material conforms to the chemical description on the

label. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW,

BAYER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY,

INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF

FITNESS OR MERCHANTABILITY, and no agent of Bayer is

authorized to do so except in writing with a specific reference

to this warranty. Any damages arising from a breach of this

warranty shall be limited to direct damages and shall not

include consequential commercial damages such as loss of

profits or values, etc.

Manufactured For  
Bayer HealthCare LLC, Animal Health Division,  
P.O. Box 390, Shawnee Mission, Kansas 66201 USA  
Bayer, the Bayer Cross and Advantage are registered  
trademarks of Bayer

© 2009 Bayer HealthCare LLC

Made in Germany

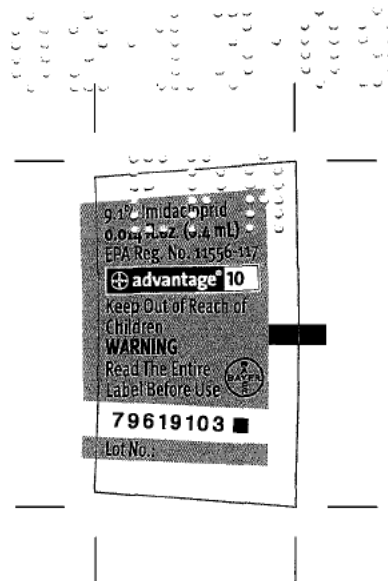
Advantage is protected by the following U.S. patents:

6,232,328 and 6,001,858

79619758  
00837885-032899/01791706-053899, R.13  
EPA Est. No. 11556-DEU-1  
EPA Reg. No. 11556-117



## Bayer HealthCare



<b>LSD GmbH &amp; Co. KG</b> In der Steele 13 · 40599 Düsseldorf Tel.: 0211-7 48 49-0 · Fax: -410	<b>PM no.:</b> 79619103 <b>CR no.:</b> 006393 <b>Format:</b> 20,5 x 35 mm <b>Font size:</b> 6 pt <b>Drawing no.:</b> 6101E		Bayer Animal Health GmbH <b>approved by BAH-PS-TO/PT</b>		<b>In case of questions</b> phone: +49 2173 38...	
	<b>Colours:</b> <b>Schwarz</b> Pantone 346 Pantone 349 Stanze		<b>Technology</b> on ..... by .....		<b>Technology:</b> Thomas Fromm (VTFRT)..... 4702 Jörg Habig (TGHAJ)..... 5519 Uwe Müller (TGMUE)..... 4614 Otto Wilinski (VTWIL)..... 4701	
			<b>Text + Layout</b> on ..... by .....		<b>Text + Presentation:</b> Christina Höfer (PHJNC)..... 4724 Rita Felicitas Reich (VTRER)..... 4098 Yvonne Sabatini (TGYVO)..... 4082 Renate Steinacker (VTSTE)..... 3046	
This proof is NOT a true representation of the final colours that will be printed.						

# Material to be added to an e-Jacket/Jacket

Reg. No. 11556-117

Description: \_\_\_\_\_

1. ☐ Placement within the e-Jacket/jacket:

☒ Default: (chronological, top = newest)

☐ File Location: (PDF page number, i.e., "before page 45")

\_\_\_\_\_  
\_\_\_\_\_

2. ☐ Send to Data Extraction contractors this material:

☒ Newly stamped accepted label 12/30/08

☐ Notification

☒ New CSF

12/30/08

☐ Other: \_\_\_\_\_

3. Attach this coversheet to the top of the material or jacket. It must be well organized and clipped together, NOT STAPLED. Then give the material with this coversheet to staff in the Information Services Center (Room S-4900).

Reviewer's Name: Autumn Metzger  
703-

Phone: 305-5314 Division: RD-1RB

Date: 12/30/08



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460



OFFICE OF  
PREVENTION, PESTICIDES,  
AND TOXIC SUBSTANCES

JAN 05 2009

Douglas Spilker, Ph.D  
Bayer HealthCare LLC, Animal Health Division  
P.O. Box 390  
Shawnee Mission, KS 66201-0390

Dear Dr. Spilker:

Subject: Proposed Change to Basic Confidential Statements of Formulation (CSF)  
Advantage Topical Flea Treatment (both Cat and Dog varieties)  
EPA Reg. Nos. 11556-116, 11556-117, 11556-118, 11556-119, 11556-120 and  
11556-122  
Your submission dated November 12, 2008

This letter is to correct the previous Agency letter dated December 29, 2008 with the incorrect product name in the subject section. The product name has been changed from "K9 Advantix" to "Advantage."

The CSFs referred to above, submitted in connection with your application for registration under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, are still acceptable. All previously dated Basic CSFs for this product are superseded and are considered obsolete. If you have any questions, please contact Autumn Metzger at (703) 305-5314 or Metzger.autumn@epa.gov.

Regards,

A handwritten signature in cursive script that reads "Venus Eagle".

Venus Eagle (PM 01)  
Insecticide-Rodenticide Branch  
Registration Division (7505P)

**\*Product ingredient source information may be entitled to confidential treatment\***



Doug Spilker  
<doug.spilker.b@bayer.com>

01/05/2009 11:17 AM

To Autumn Metzger/DC/USEPA/US@EPA

cc

bcc

Subject Advantage Topical Solution (EPA Reg. Nos. 11556-116, -117, -118, 119, -120, 122)

Hi Autumn,  
Happy New Year! Hope you had some good time off. I'm glad I left myself a To Do list for when I got back. I was off for 2 weeks.

Thanks for the Acceptance letter of the revised CSFs for the subject products (see attached). That's good news for our production people. However, I was wondering if you could help me out on something. We will send this acceptance notification to several colleagues notifying them that this is the new standard. I will send a copy to our production colleagues in [REDACTED]. Unfortunately the Subject line of your acceptance letter is a little confusing. I understand by the listed Reg. numbers that the acceptance is for our Advantage Topical Solution products, but the Subject line says Advantix. We sell products named both Advantage and K9 Advantix, and there is a lot of confusion between the two lines of products. Also, Advantage does not control ticks.

Might it be possible to reissue the acceptance letter with the correct Advantage product name? Sorry to hit you with this right at after the first of the year, but it would really help to get this cleared up before I start distributing the acceptance to my colleagues.

Thanks, and call if you have any questions.  
best regards,

Doug

Doug Spilker  
Manager - EPA Reg. Affairs  
BAYER HEALTHCARE LLC  
ANIMAL HEALTH  
Office: +1 913-268-2751  
Mobile: +1 816-506-3102  
Fax: +1 913-268-2135  
Email: doug.spilker.b@bayer.com

Address:  
P.O. Box 390  
Shawnee Mission, KS 66201-0390  
Country: USA

Bayer Animal Health "Powered by People, Driven by Science"

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460



OFFICE OF  
PREVENTION, PESTICIDES,  
AND TOXIC SUBSTANCES

DEC 29 2008

Douglas Spilker, Ph.D  
Bayer HealthCare LLC, Animal Health Division  
P.O. Box 390  
Shawnee Mission, KS 66201-0390

Dear Dr. Spilker:

Subject: Proposed Change to Basic Confidential Statements of Formulation (CSF)  
Advantix Topical Flea/Tick Treatment  
EPA Reg. Nos. 11556-116, 11556-117, 11556-118, 11556-119, 11556-120 and  
11556-122  
Your submission dated November 12, 2008

The CSFs referred to above, submitted in connection with your application for registration under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, is acceptable. All previously dated Basic CSFs for this product are superseded and are considered obsolete. If you have any questions, please contact Autumn Metzger at (703) 305-5314 or Metzger.autumn@epa.gov.

Regards,

*Venus Eagle*

Venus Eagle (PM 01)  
Insecticide-Rodenticide Branch  
Registration Division (7505P)

**UNITED STATES ENVIRONMENTAL PROTECTION AGENCY**  
WASHINGTON, D.C. 20460



OFFICE OF  
PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES

December 24, 2008

Both Sami from TRB and John Hebert (PM07) verbally accepted lowering the certified limits of the [REDACTED] on the CSFs.

Autumn Metzger

A handwritten signature in black ink, appearing to be "AM", written over a horizontal line.

**\*Inert ingredient information may be entitled to  
confidential treatment\***

# Receipt for Section 3

S: 839894

Resubmission: ☐ Yes ☒ No

Regulatory Type: Product Registration - Section 3

Free For Service: ☐ Yes ☒ No

Application Type: Amendment

Billable: ☐ Yes ☒ No

Company: 11556 BAYER HEALTHCARE LLC V


Risk Manager: Registration Division, Risk Management Team 1


Product #: 11556-117 Product Name: ADVANTAGE TM 1D (IMIDACLOPRID) TOPICAL


Overdose:

Me Too Section3: Me Too Product Name:

Application Date: 10-Nov-2008 

OPP Rec'd Date: 12-Nov-2008 

Front End Date: 13-Nov-2008 

Risk Manager Send Date: 17-Nov-2008 

FFS Due Date:

Negotiated Due Date:

OPP Target Date:

Fast Track: ☐ New Ingredient: ☐

Receipt Description:

CSF amendment

New Ingredient:

Product Name:

New Ingredient:

Received Date:

Form A: ☐ Signature Date:

Form B: ☐ Signature Date:

Print Letter

Enter More Information

Tracking

Receipt Content



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

November 17, 2008

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

TERRY MCNAMARA  
BAYER HEALTHCARE LLC  
ANIMAL HEALTH DIVISION  
PO Box 390  
SHAWNEE MISSION, KS 66201-0390

PRODUCT NAME: ADVANTAGE TM 10 (IMIDACLOPRID) TOPICAL SOLUTION  
COMPANY NAME: BAYER HEALTHCARE LLC  
OPP IDENTIFICATION NUMBER:  
EPA FILE SYMBOL: 11556-117  
EPA RECEIPT DATE: 11/12/08

SUBJECT: RECEIPT OF AMENDMENT

DEAR REGISTRANT:

The Office of Pesticide Programs has received your application for an amendment and it has passed an administrative screen for completeness.

During the initial screen we determined that the application appears to qualify for fast track review. The package will now be forwarded to the Product Manager for review to determine its acceptability for fast track status.

If you have any questions, please contact Registration Division, Risk Management Team 1, at (703) 308-8045.

Sincerely,

*P. H. Moore*  
Front End Processing Staff  
Information Services Branch  
Information Technology & Resources Management Division

MIN Bod - CETS PM-01

# FAST-TRACK AMENDMENTS-Completeness Screening Checklist

Experts In-Processing Signature: Autumn Metzger

EPA Reg. Number: <u>11556-117</u>		EPA Receipt Date: <u>11-12-08</u>		
	Check List Item	Yes	No	NA
1	<b>Application Form</b> (EPA Form 8570-1) -signed?	✓		
2	<b>Confidential Statement of Formula</b> (EPA Form 8570-29) - signed?	✓		
3	<b>Certification with Respect to Citation of Data</b> (EPA Form 8570-34) signed?			✓
4	<b>Formulator's Exemption Statement</b> (EPA Form 8570-27) - signed?			✓
5	<b>Data Matrix</b> (EPA Form 8570-35) [Applicable, for adding me-too uses]			✓
	a) Selective Method?			
	b) Cite-All Method? Applicant owns data or list only the companies offered to pay			
	c) Public copy of Matrix provided? See PR Notice 98-5			
6	<b>Is Label Included?</b> (5 copies)		✓	
<b>Comments:</b>  <div style="font-size: 1.5em; margin-top: 50px;">1 letter cleared</div>				

Autumn

## Fee for Service

*pen M*  
{839894b~

This package includes the following

- ☐ New Registration
- ☒ Amendment

- ☐ Studies?      ☐ Fee Waiver?
- ☐ volpay    % Reduction: \_\_\_\_

for Division

- ☐ AD
- ☐ BPPD
- ☒ RD

Risk Mgr. 1

Receipt No.

S-

839894

EPA File Symbol/Reg. No.

11556-117

Pin-Punch Date:

11/12/2008



This item is NOT subject to FFS action.

### Action Code:

Requested:

Granted:

Amount Due: \$ \_\_\_\_

### Parent/Child Decisions:

*Inerts approved for non-food use*  
☒ Inert Cleared for Intended Use

☐ Uncleared Inert in Product

Reviewer:

J. Miller

Date: 11-14-08

Remarks:



*Via Federal Express*

November 10, 2008

Document Processing Desk  
**(Fast Track Amendment – Non-PRIA Action)**  
Office of Pesticide Programs (7504P)  
U.S. Environmental Protection Agency  
Room S-4900, One Potomac Yard  
2777 South Crystal Drive  
Arlington, VA 22202-4501

Attention: Ms. Venus Eagle, PM Team 01  
Registration Division

Advantage 10 (EPA Reg. 11556-117)

- a. Form 8570-1 Application for Amendment
- b. Attachment to Application (2 pages)
- c. Confidential Statement of Formula, dated 11/06/08 (2 copies)
- d. Confidential Statement of Formula, dated 5/30/95 (superseded)

**\*Inert ingredient information may be entitled to confidential treatment\***

Print Form

Please read instructions on reverse before completing form.

Form Approved. OMB No. 2070-0060. Approval expires 2-28-



United States  
**Environmental Protection Agency**  
Washington, DC 20460

☐ Registration  
☒ **Amendment**  
☐ Other

OPP Identifier Number

**Application for Pesticide - Section I**

1. Company/Product Number 11556-117	2. EPA Product Manager Venus Eagle	3. Proposed Classification <input checked="" type="checkbox"/> None <input type="checkbox"/> Restricted
4. Company/Product (Name) Advantage 10 Topical Solution	PM# Team 1	
5. Name and Address of Applicant (Include ZIP Code) Bayer HealthCare LLC, Animal Health Division P. O. Box 390 Shawnee Mission, KS 66201-0390  <input type="checkbox"/> Check if this is a new address	6. <b>Expedited Review.</b> In accordance with FIFRA Section 3(c)(3) (b)(i), my product is similar or identical in composition and labeling to: EPA Reg. No. _____  Product Name _____	

**Section - II**

<input checked="" type="checkbox"/> Amendment - Explain below.	<input type="checkbox"/> Final printed labels in response to Agency letter dated _____
<input type="checkbox"/> Resubmission in response to Agency letter dated _____	<input type="checkbox"/> "Me Too" Application.
<input type="checkbox"/> Notification - Explain below.	<input type="checkbox"/> Other - Explain below.

**Explanation:** Use additional page(s) if necessary. (For section I and Section II.)

Enclosed for Agency acceptance are 2 copies of the Confidential Statement of Formula, dated 11/06/08, revised to lower the certified limit of the [REDACTED] and update other information. Please see attached for further information. Minor formulation change (no data to review); Non-PRIA action.

**Section - III**

1. Material This Product Will Be Packaged In:				2. Type of Container	
Child-Resistant Packaging <input type="checkbox"/> Yes <input type="checkbox"/> No	Unit Packaging <input type="checkbox"/> Yes <input type="checkbox"/> No	Water Soluble Packaging <input type="checkbox"/> Yes <input type="checkbox"/> Text <input type="checkbox"/> No		<input type="checkbox"/> Metal <input type="checkbox"/> Plastic <input type="checkbox"/> Glass <input type="checkbox"/> Paper <input type="checkbox"/> Other (Specify) _____	
* Certification must be submitted		If "Yes" Unit Packaging wgt.	No. per container	If "Yes" Package wgt	No. per container
3. Location of Net Contents Information <input type="checkbox"/> Label <input type="checkbox"/> Container		4. Size(s) Retail Container		5. Location of Label Directions <input type="checkbox"/> On Label <input type="checkbox"/> On Labeling accompanying product	
6. Manner in Which Label is Affixed to Product <input type="checkbox"/> Lithograph <input type="checkbox"/> Paper glued <input type="checkbox"/> Stenciled		<input type="checkbox"/> Other _____			

**Section - IV**

1. Contact Point (Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)		
Name Douglas A. Spilker, Ph. D. (doug.spilker.b@bayer.com)	Title Manager, EPA Regulatory Affairs	Telephone (Include Area Code) 913-268-2751
<b>Certification</b> I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.		8. Date Application Received (Stamped)
2. Signature 	3. Title Manager, EPA Regulatory Affairs	
4. Typed Name Douglas A. Spilker, Ph. D.	5. Date 10 Nov. 2008	70

ATTACHMENT FOR OPP  
APPLICATION FOR PESTICIDE AMENDMENT  
Page 1 of 3

**Advantage 10 Topical Solution, EPA Reg. No. 11556-117**  
**November 6, 2008**

Enclosed for Agency acceptance are two (2) copies of the draft **Confidential Statement of Formula**, dated November 6, 2008 for Advantage 10 Topical Solution, EPA Reg. No. 11556-117, which supersedes the current CSF on file with the Agency, dated May 30, 1995 (attached).

The proposed changes are described below:

Block 1. Update Name of Applicant/Registrant

from: Bayer Corporation  
Agriculture Division  
Animal Health  
to: Bayer HealthCare LLC, Animal Health Division

Block 3. Include the Complete Product Name (not a name change)

from: Advantage 10  
to: Advantage 10 Topical Solution

Block 4. Complete Registration No.

from: 11556-  
to: 11556-117

Block 5. Update EPA Product Mgr/Team No.

from: Edwards/19  
to: V. Eagle/01

Block 10. Correct Component Name for Imidacloprid Technical

from: NTN 33893 Technical Pesticide Imidacloprid or  
1-[(6-chloro-3-pyridinyl) methyl]-N-nitro-2-imidazolodininime  
to: Imidacloprid Technical 98%

Block 11. Provide Supplier Name & Address for Imidacloprid Technical

from: no information provided  
to: Bayer CropScience  
P.O. Box 12014  
2 TW Alexander Dr.  
Research Triangle Park, NC 27709

**\*Product ingredient source information may be  
entitled to confidential treatment\***

Block 11. Provide Supplier Name & Address for

from: no information provided  
to:

**\*Inert ingredient information may be  
entitled to confidential treatment\***

ATTACHMENT FOR OPP  
APPLICATION FOR PESTICIDE AMENDMENT  
Page 2 of 3

Advantage 10 Topical Solution, EPA Reg. No. 11556-117  
November 6, 2008

Block 11. Provide Supplier Name & Address for

from: no information provided

to:

Block 11. Update Supplier Name & Address for

from: no information provided

to:

Block 12. Update EPA Reg. No.

from: 3125-414

to: 264-755

Block 14. Change the Lower Certified Limit for

from:

to:

Block 16. Update Typed Name of Approving Official

from: F. T. McNamara

to: Jochem Rueter

Block 18. Update Signature of Approving Official

from: F. T. McNamara

to: Jochem Rueter

Block 19. Update Title

from: Biochemistry & Pesticide Registrations Mgr.

to: Director, Technical Development

\*Product ingredient source information may be entitled to  
confidential treatment\*

\*Inert ingredient information may be  
entitled to confidential treatment\*

ATTACHMENT FOR OPP  
APPLICATION FOR PESTICIDE AMENDMENT  
Page 3 of 3

**Advantage 10 Topical Solution, EPA Reg. No. 11556-117**  
**November 6, 2008**

Block 20. Update Phone No.

from: no information provided  
to: 913-268-2046

Block 21. Update the Date

from: 5/30/95  
to: Nov. 6, 2008

**UNITED STATES ENVIRONMENTAL PROTECTION AGENCY**

WASHINGTON, D.C. 20460



NOV 04 2008

OFFICE OF  
PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES

Douglas Spilker, Ph.D  
Bayer HealthCare LLC, Animal Health Division  
P.O. Box 390  
Shawnee Mission, KS 66201-0390

Dear Dr. Spilker:

Subject: Amendment of label to revise according to EPA's letter of 3/4/08, PR Notice  
2007-4 and other minor changes  
Advantage® 9 & 10 Topical Solutions  
EPA Registration No. 11556-116 & 11556-117  
Your Email Re-submissions were received 10/29/08

The labeling referred to above submitted in connection with the Federal Insecticide,  
Fungicide and Rodenticide, as amended are acceptable.

A stamped copy of the labeling is enclosed for your records. Please submit one final  
printed copy of the labeling before releasing the product for shipment. If you have any questions  
regarding this label, please contact Autumn Metzger at (703) 305-5314.

Sincerely,

A handwritten signature in cursive script that reads "Venus Eagle".

Venus Eagle  
Product Manager 01  
Insecticide-Rodenticide Branch  
Registration Division (7505P)

Reason To Issue: Revise according to EPA letter of Date: 09/05/08  
03/04/2008, and make other minor changes. Supersedes: 02/04/08

Note to Reviewer: [Brackets and parentheses indicate alternate language]

## **Advantage® 10 Topical Solution**

Once-A-Month Topical Flea and Lice Treatment For [Small] Dogs and  
Puppies 7 Weeks and Older and 10 lbs and Under.

### **READ THE ENTIRE LABEL BEFORE EACH USE**

For the Prevention and Treatment of Flea and Lice Infestations on Dogs

- One treatment prevents further flea infestation for at least four (4) weeks
- Kills fleas on dogs within 12 hours
- Kills fleas before they lay eggs
- Convenient, easy to apply
- Kills [(biting) (chewing)] lice
- For treatment and prevention of [(biting) (chewing)] lice [infestations]
- Controls existing [(biting) (chewing)] lice infestations
- Dual protection (against fleas and lice)
- Treats, prevents and controls [(biting) (chewing)] lice [infestations]
- Provides effective control of [(biting) (chewing)] lice [infestations]
- Kills [(biting) (chewing)] lice and prevents further infestations
- For treatment and prevention of infestations with [(biting) (chewing)] lice
- Waterproof
- Fragrance free

	<u>% By Weight</u>
Active Ingredient	
Imidacloprid .....	9.1%
Other Ingredients .....	90.9%
Total .....	100.0%

**EPA Reg. No. 11556-117**

**EPA Est. No. 11556-DEU-1**

### **KEEP OUT OF REACH OF CHILDREN**

[For Directions For Use, and Storage and Disposal (instructions),  
see supplemental labeling inside]

**ACCEPTED**

**NOV 04 2008**

Under the Federal Insecticide, Fungicide,  
and Rodenticide Act, as amended, for the  
pesticide registered under:

### WARNING

See Below for First Aid and Precautionary Statements

### PRECAUTIONARY STATEMENTS

**HAZARDS TO HUMANS:** Causes eye irritation. Harmful if swallowed. Do not get in eyes or on clothing. Avoid contact with skin. Wash hands thoroughly with soap and warm water after handling. Keep out of reach of children. Do not contaminate feed or food.

### HAZARDS TO DOMESTIC ANIMALS

**For external use only.** Do not use on puppies under seven weeks of age. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing animals. Individual sensitivities, while rare, may occur after using ANY pesticide product for pets. If signs persist, or become more severe, consult a veterinarian immediately. If your animal is on medication, consult your veterinarian before using this or any other product. For consumer questions call 1-800-255-6826. For medical emergencies call 1-800-422-9874.

### FIRST AID

Have the product container or label with you when calling a poison control center or doctor, or going for treatment.

**If in eyes:** Hold eye open and rinse slowly and gently with water for 15 – 20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.

**If swallowed:** Call poison control center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by the poison control center or doctor. Do not give anything by mouth to an unconscious person.

**If on skin or clothing:** Take off contaminated clothing. Rinse skin immediately with plenty of water for 15 – 20 minutes. Call a poison control center or doctor for treatment advice.

**To Physician:** Treat the patient symptomatically.

### DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling.



## HOW TO APPLY

1. Use only on dogs. Do not use on other animals.
2. Remove one applicator tube from the package.

[Visuals Depicting How to Open Applicator Tube]

3. Hold applicator tube in an upright position. Pull cap off tube.
4. Turn the cap around and place other end of cap back on tube.
5. Twist cap to break seal, then remove cap from tube.

[Visuals Depicting Application To Animal]

6. The dog should be standing for easy application. Part the hair on the dog's back, between the shoulder blades, until the skin is visible. Place the tip of the tube on the skin and squeeze the tube to *expel the entire contents directly on the skin.*

*Do not get this product in your pet's eyes or mouth.*

7. Discard empty tube as described in Storage and Disposal.
8. In case of severe flea infestation, retreatment may be necessary earlier than four weeks. Do not retreat more often than once every seven days. After flea control is attained, return to a monthly retreatment schedule.

## GENERAL INFORMATION

The successive feeding activity of fleas on pets may elicit a hypersensitivity skin disorder known as flea allergy dermatitis (FAD). Treatment of dogs with Advantage kills fleas and may reduce the incidence of this condition.

Advantage kills fleas on dogs within 12 hours. Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting for up to four (4) weeks. Pre-existing pupae in the environment may continue to emerge for six (6) weeks or longer depending upon the climatic conditions.

Larval flea stages in the pet's surroundings are killed following contact with an Advantage treated pet.

Advantage is waterproof and remains effective following a shampoo treatment, swimming or after exposure to rain or sunlight.

Monthly treatments are required for optimal control and prevention of fleas.

## **STORAGE AND DISPOSAL**

Do not contaminate water, food or feed by storage or disposal.

**Storage:** Store in a cool, dry place.

**Disposal:** Nonrefillable container. **If empty:** Do not reuse or refill this container. Place in trash or offer for recycling if available.

**If partly filled:** Call your local solid waste agency or 1-800-422-9874 for disposal instructions. Never place unused product down any indoor or outdoor drain.

## **LIMITED WARRANTY AND LIMITATION OF DAMAGES**

Bayer HealthCare LLC, Animal Health Division warrants that this material conforms to the chemical description on the label. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, BAYER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY, INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR MERCHANTABILITY, and no agent of Bayer is authorized to do so except in writing with a specific reference to this warranty. Any damages arising from a breach of this warranty shall be limited to direct damages and shall not include consequential commercial damages such as loss of profits or values, etc.

Four [or six] 0.014 fl. oz (0.4 mL) Tubes

Manufactured For

Bayer HealthCare LLC  
Animal Health Division

P.O. Box 390

Shawnee Mission, Kansas 66201 USA

Made in Germany

Reason To Issue: Revise according to EPA letter of  
03/04/2008, and make other minor changes.

Date: 09/05/08  
Supersedes: 02/04/08

---

[Label on Individual Tube]

Advantage® 10

9.1% Imidacloprid

0.014 fl. oz. (0.4 mL)

EPA Reg. No. 11556-117

Warning

Keep Out of Reach of Children

Read The Entire Label Before Use

BAYER

Lot No. 0000000



Doug Spilker  
<doug.spilker.b@bayer.com>

10/29/2008 03:59 PM

To Autumn Metzger/DC/USEPA/US@EPA

cc

bcc

Subject Advantage revised labels

Re-submission S 839272

Hi Autumn,

As your email below requests, please find attached PDF versions of our draft labeling for the six (6) Advantage products.

For the two on your desk currently awaiting acceptance (EPA REG Nos. 11556-116 and 11556-117), please find attached clean copies of each with only the requested changes. No other changes have been made. You will note that the date of draft has not changed from the date on the original submission (09/05/08), since it is my understanding that you will substitute the attached revised versions for the previously submitted ones.

For the four products that were already accepted (EPA REG Nos. 11556-118, -119, -120 and -122), we understand that you will process the attached labels with no additional paperwork from us, "...since you are requiring the change." Please find attached clean copies of each with only the requested changes. You will note that the date of draft has changed from the date on the original submission (09/05/08) to today's date, since the Agency had already accepted the previous version.

If our understandings are incorrect, or you need something further, please do not hesitate to call.

Best regards,

Doug

Doug Spilker  
Manager - EPA Reg. Affairs  
BAYER HEALTHCARE LLC  
ANIMAL HEALTH  
Office: +1 913-268-2751  
Mobile: +1 816-506-3102  
Fax: +1 913-268-2135  
Email: doug.spilker.b@bayer.com

Address:  
P.O. Box 390  
Shawnee Mission, KS 66201-0390  
Country: USA

Bayer Animal Health "Powered by People, Driven by Science"

Metzger.Autumn@epamail.epa.gov

10/29/2008 11:21 AM

To: doug.spilker.b@bayer.com  
cc:

Subject Re: Fw: Advantage Re-treatment Language

Hello Doug,

Venus has approved your new label language. For the 4 that were already approved, we will take care of the processing on our end (since we are requiring the change) if you could send us a "clean" label with this adjustment, along with the adjustments required on the letter I sent you (and no other changes).

For the two on my desk currently awaiting approval (EPA REG NOS 11556-117 & 11556-116) Please send me clean copies of each with only the following changes:

On page 4, revise the first statement, "If re-treatment becomes necessary earlier than four weeks, do not re-treat more than once weekly" to the agreed upon statement: "In case of severe flea infestation, retreatment may be necessary earlier than four weeks. Do not retreat more often than once every seven days. After flea control is attained, return to a monthly retreatment schedule .", Since the above statement is mandatory, it cannot be included under "General Information." Move it into the "Directions for Use" area. It is also recommended that you move the EPA Reg. Number and EPA Est. Numbers to the first page.

Please send me all clean copies threw email in pdf format. Thanks for all your help! I hope to get them all completed quickly.

Also - I believe my email did just change to: metzger.autumn@epa.gov (that may have been why it was bouncing back b/c it was in the process of changing) If you still have trouble send to to Venus again and call me to let me know so I can get them from her.

Thanks!

Autumn Bonomi-Metzger  
Biologist  
U.S. Environmental Protection Agency  
Insecticide-Rodenticide Branch  
Registration Division (7505P)  
1200 Pennsylvania Ave. NW  
Washington, DC 20460

Tel: 703 305-5314  
Fax: 703 308-5433  
Email: bonomi.autumn@epa.gov

Venus  
Eagle/DC/USEPA/U  
S

10/29/2008 11:44  
AM

To  
Autumn Metzger/DC/USEPA/US@EPA  
cc  
Subject  
Fw: Advantage Re-treatment  
Language

I'm OK with this revised language now. Please add the exact language to the remaining two products.

Thanks,

Venus,

---

Venus Eagle  
Product Manager (01)  
Insecticide-Rodenticide Branch  
Registration Division  
(703) 308-8045

----- Forwarded by Venus Eagle/DC/USEPA/US on 10/29/2008 11:43 AM -----

Doug Spilker  
<doug.spilker.b@  
bayer.com>

10/29/2008 09:04  
AM

To  
Venus Eagle/DC/USEPA/US@EPA,  
Autumn Metzger/DC/USEPA/US@EPA  
cc  
Terry McNamara  
<terry.mcnamara.b@bayer.com>  
Subject  
Advantage Re-treatment Language

Dear Autumn and Venus,  
Thank you for your voice mail of October 22 in response to my email of earlier that day, regarding the Advantage retreatment statement on the two pending labels (text dated 09/05/08) and the four labels previously accepted on 09/18/08. It is our understanding that the Agency would like further clarification on these labels on when retreatment would be

necessary. This email is in response to that request.

Our current labels allow for weekly retreatment, if necessary. Although you may not be aware of the history, the one-week retreatment interval for Advantage products is based upon the weekly retreatment intervals used in the Advantage companion animal safety studies. Briefly, in the EPA-accepted domestic animal safety studies on dogs (Bayer Report No. 74590; MRID 43679608), puppies (74730; 44099801), cats (74591; 43679502) and kittens (74747; 44157302), the animals were treated with 5X treatments at weekly intervals for eight (8) consecutive weeks. All four studies were found acceptable to support the registration of the products with the current retreatment statement. So, from a safety viewpoint, the data clearly support retreatment as frequently as once per week.

However, from an efficacy viewpoint Advantage was designed as a once-a-month product. There are unusual situations where retreatment may be necessary to provide complete control. Accordingly, we propose the following revised retreatment statement for your consideration:

"In case of severe flea infestation, retreatment may be necessary earlier than four weeks. Do not retreat more often than once every seven days. After flea control is attained, return to a monthly retreatment schedule ."

Bayer feels that this label language further refines the retreatment instructions, and improves the use directions.

If further discussion is needed on the proposed revision, please do not hesitate to call.

best regards,  
Doug

Doug Spilker, Ph.D.  
Manager - EPA Reg. Affairs  
BAYER HEALTHCARE LLC  
ANIMAL HEALTH  
Office: +1 913-268-2751  
Mobile: +1 816-506-3102  
Fax: +1 913-268-2135  
Email: doug.spilker.b@bayer.com

Address:  
P.O. Box 390  
Shawnee Mission, KS 66201-0390  
Country: USA

Bayer Animal Health "Powered by People, Driven by Science"

The information contained in this e-mail is for the exclusive use of the intended recipient(s) and may be confidential, proprietary, and/or legally privileged. Inadvertent disclosure of this message does not constitute a waiver of any privilege. If you receive this message in error, please do not directly or indirectly use, print, copy, forward, or disclose any part of this message. Please also delete this e-mail and all copies and notify the sender. Thank you.

# FAST-TRACK AMENDMENTS-Completeness Screening Checklist

Experts In-Processing Signature: B. Alexander

EPA Reg. Number: <u>11556-117</u>		EPA Receipt Date: <u>9-8-2008</u>		
	Check List Item	Yes	No	NA
1	Application Form (EPA Form 8570-1) -signed?	<input checked="" type="checkbox"/>		
2	Confidential Statement of Formula (EPA Form 8570-29) - signed?			<input checked="" type="checkbox"/>
3	Certification with Respect to Citation of Data (EPA Form 8570-34) signed?			<input checked="" type="checkbox"/>
4	Formulator's Exemption Statement (EPA Form 8570-27) - signed?			<input checked="" type="checkbox"/>
5	Data Matrix (EPA Form 8570-35) [Applicable, for adding me-too uses]			<input checked="" type="checkbox"/>
	a) Selective Method?			
	b) Cite-All Method? Applicant owns data or list only the companies offered to pay			
	c) Public copy of Matrix provided? See PR Notice 98-5			
6	Is Label Included? (5 copies)	<input checked="" type="checkbox"/>		
	Comments:			





UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

September 9, 2008

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

TERRY MCNAMARA  
BAYER HEALTHCARE LLC  
ANIMAL HEALTH DIVISION  
PO Box 390  
SHAWNEE MISSION, KS 66201-0390

PRODUCT NAME: ADVANTAGE TM 10 (IMIDACLOPRID) TOPICAL SOLUTION  
COMPANY NAME: BAYER HEALTHCARE LLC  
OPP IDENTIFICATION NUMBER:  
EPA FILE SYMBOL: 11556-117  
EPA RECEIPT DATE: 09/08/08

SUBJECT: RECEIPT OF AMENDMENT

DEAR REGISTRANT:

The Office of Pesticide Programs has received your application for an amendment and it has passed an administrative screen for completeness.

During the initial screen we determined that the application appears to qualify for fast track review. The package will now be forwarded to the Product Manager for review to determine its acceptability for fast track status.

If you have any questions, please contact Registration Division, Risk Management Team 1, at (703) 308-8045.

Sincerely,

*P. H. Moore*  
Front End Processing Staff  
Information Services Branch  
Information Technology & Resources Management Division

## Fee for Service

*rem*  
*M*  
{835682=~

This package includes the following

- ☐ New Registration
- ☒ Amendment

☐ Studies?      ☐ Fee Waiver?  
☐ volpay    % Reduction: \_\_\_\_

for Division

- ☐ AD
- ☐ BPPD
- ☒ RD

Risk Mgr. 1

Receipt No.

S-

835682

EPA File Symbol/Reg. No.

11556-117

Pin-Punch Date:

9/8/2008

☒ This item is NOT subject to FFS action.

### Action Code:

Requested:

Granted:

Amount Due: \$ \_\_\_\_

### Parent/Child Decisions:

☐ Inert Cleared for Intended Use

☐ Uncleared Inert in Product

Reviewer: *gpl*

Date: 9/9/08

Remarks:

Please read instructions on reverse before completing form.

Form Approved. OMB No. 2070-0060. Approval expires 2-28-



United States  
Environmental Protection Agency  
Washington, DC 20460

☐ Registration  
☒ Amendment  
☐ Other

OPP Identifier Number

## Application for Pesticide - Section I

1. Company/Product Number 11556-117	2. EPA Product Manager Venus Eagle	3. Proposed Classification <input checked="" type="checkbox"/> None <input type="checkbox"/> Restricted
4. Company/Product (Name) Advantage 10 Topical Solution	PM# Team 1	
5. Name and Address of Applicant (Include ZIP Code) Bayer HealthCare LLC, Animal Health Division P. O. Box 390 Shawnee Mission, KS 66201-0390  <input type="checkbox"/> Check if this is a new address	6. Expedited Review. In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to: EPA Reg. No. _____  Product Name _____	

## Section - II

<input checked="" type="checkbox"/> Amendment - Explain below.	<input type="checkbox"/> Final printed labels in response to Agency letter dated _____
<input type="checkbox"/> Resubmission in response to Agency letter dated _____	<input type="checkbox"/> "Me Too" Application.
<input type="checkbox"/> Notification - Explain below.	<input type="checkbox"/> Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Enclosed for Agency acceptance are 5 copies of the draft labeling, dated 09/05/08, amended to revise according EPA's letter of 03/04/08, PR Notice 2007-4 and make other minor changes. Please see attached for further information. There are no data to review, so this is a Non-PRIA action.

## Section - III

1. Material This Product Will Be Packaged In:				2. Type of Container	
Child-Resistant Packaging <input type="checkbox"/> Yes <input type="checkbox"/> No	Unit Packaging <input type="checkbox"/> Yes <input type="checkbox"/> No	Water Soluble Packaging <input type="checkbox"/> Yes <input type="checkbox"/> Text <input type="checkbox"/> No		<input type="checkbox"/> Metal	<input type="checkbox"/> Plastic
* Certification must be submitted				<input type="checkbox"/> Glass	<input type="checkbox"/> Paper
	If "Yes" Unit Packaging wgt.	No. per container	If "Yes" Package wgt	No. per container	Other (Specify) _____
3. Location of Net Contents Information <input type="checkbox"/> Label <input type="checkbox"/> Container		4. Size(s) Retail Container		5. Location of Label Directions <input type="checkbox"/> On Label <input type="checkbox"/> On Labeling accompanying product	
6. Manner in Which Label is Affixed to Product <input type="checkbox"/> Lithograph <input type="checkbox"/> Paper glued <input type="checkbox"/> Stenciled		<input type="checkbox"/> Other _____			

## Section - IV

1. Contact Point (Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)		
Name Douglas A. Spilker, Ph. D. [doug.spilker.b@bayer.com]	Title Manager, EPA Regulatory Affairs	Telephone No. (Include Area Code) 913-268-2751
<b>Certification</b> I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.		C. Date Application Received (Stamped)
2. Signature 	3. Title Manager, EPA Regulatory Affairs	
4. Typed Name Douglas A. Spilker, Ph. D.	5. Date 5 Sept 2008	

*Via Federal Express*

September 5, 2008

Document Processing Desk  
**(Fast Track Amendment – Non-PRIA Action)**  
Office of Pesticide Programs (7504P)  
U.S. Environmental Protection Agency  
Room S-4900, One Potomac Yard  
2777 South Crystal Drive  
Arlington, VA 22202-4501

Attention: Ms. Venus Eagle, PM Team 01  
Registration Division

Advantage 10 (EPA Reg. 11556-117)

- a. Form 8570-1 Application for Amendment
- b. Attachment to Application (2 pages)
- c. Draft Labels, dated 9/05/2008 (5 copies)
- d. Draft Label (highlighted), dated 09/05/2008 (1 copy)
- e. EPA Stamped-Accepted Labeling, acceptance date March 4, 2008

Attachment to:  
OPP APPLICATION FOR PESTICIDE – AMENDMENT

**Section II – Explanation:**

Enclosed for the Agency's acceptance are five (5) copies of the revised draft labels, dated September 5, 2008, for Advantage 10 Topical Solution, EPA Reg. No. 11556-117. Enclosed is an identical copy of the aforementioned draft label, with the respective revisions highlighted for the Agency's convenience. The enclosed draft labeling is identical to the labeling accepted by the Agency on March 4, 2008 (copy enclosed), with the following changes:

**A. Page 1:**

- 1) Removal of the parenthetical phrase "(imidacloprid)" from the product name line; this is not needed since the active ingredient is listed in the ingredient statement and "imidacloprid" is not a part of the official product name as registered with EPA.
- 2) Removal of the bulleted statement on page 1 that reads "Available only through licensed practicing veterinarians" to make the packaging more accurate as to how our products are distributed.
- 3) As instructed in item 1 of the Agency's letter of March 4, 2008, revision of label text to remove the "98-100%" figure from bulleted claim.
- 4) Revision of the Referral Statement to include the words "...Storage and Disposal (instructions), ..."

**B. Page 2 – No changes**

**C. Page 3:**

- 1) Removal of the graphics from the Draft Labeling that depict how to open the applicator tube and graphics depicting application to the animal. A placeholder statement appears in both spots instead, to indicate that these graphics will appear on the final printed labeling. According to the Label Review Manual (16-1) "Graphics or symbols in addition to written text are permitted on pesticide product labels if they are accompanied by explanatory text..." We currently have EPA-accepted explanatory text that appropriately describes these processes. We intend to include the respective graphics on the final printed labeling, but request this change to allow flexibility in our ability to update the graphics in subsequent printings. We will follow all Agency guidelines on this subject, as outlined in the Label Review Manual, and will submit Final Printed Labeling with these graphics as new product is produced.

2) Revise third sentence of bullet 6:

From: "Place the tip of tube on the skin and squeeze the tube **twice** to expel the entire contents of the tube directly on the skin."

To: "Place the tip of tube on the skin and squeeze the tube to expel the entire contents of the tube directly on the skin."

It is our contention that the user should determine the number of times necessary to expel the entire contents of the tube.

3) Add Sub-heading entitled "GENERAL INFORMATION"

4) As instructed in item 2 of the Agency's letter of March 4, 2008, revision of label text (paragraph 1 under GENERAL INFORMATION) to remove word "rapidly" and change word "pet" to read "dogs."

5) As instructed in item 3 of the Agency's letter of March 4, 2008, revision of label text (paragraph 2 under GENERAL INFORMATION) to remove the "98-100%" figure and change word "pet" to read "dogs."

6) Change word "efficacious" to the synonym "effective."

D. Page 4:

1) Revise "STORAGE AND DISPOSAL" section according to PR Notice 2007-4.

E. Page 5 – No changes.

FOR OFFICIAL USE ONLY

FILE SYMBOL

REGISTRATION NO.

## CONFIDENTIAL STATEMENT OF FORMULA ENCLOSED

DATE SUBMITTED	SUBMITTED BY (✓)	
	APPLICANT	BASIC SUPPLIER

**Do Not Write Comments,  
Formula, or Parts of Formula  
on This Envelope**

### NOTE

It shall be unlawful—for any person to use for his own advantage or to reveal, other than to the Secretary, or officials or employees of the United States Department of Agriculture or other Federal agencies, or to the courts in response to a subpoena, or to physicians, and in emergencies to pharmacists and other qualified persons, for use in the preparation of antidotes, in accordance with such directions as the Secretary may prescribe, any information relative to formulas of products acquired by authority of Section 4 of the "Federal Insecticide, Fungicide, and Rodenticide Act."

\*confidential statements of formula may be entitled to confidential treatment\*